Are all antianxiety-anticholinergic therapies the same?
Not if you know Librax®.

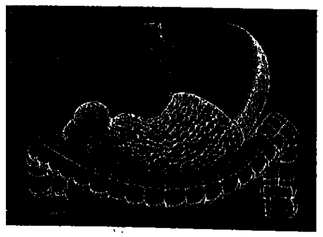


Only Librax provides

■ **the well-known antianxiety action of Librium®** (chlordiazepoxide HCl)

plus

■ **the prompt antisecretory-antispasmodic action of Quarzan®** (clidinium Br)



with the convenience and economy of a single medication… all advantages in sustaining patient compliance

adjunctive dual-action

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

For relief of psychovisceral symptoms in irritable bowel syndrome* and duodenal ulcer*

A distinctive antianxiety-anticholinergic agent

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium® (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacologic effects of agents, particularly potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are avoidable in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, *i.e.*, dryness of the mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Med Trib 27

Medical Tribune

© 1976, Medical Tribune, Inc.

and Medical News

Vol. 17, No. 27 — *world news of medicine and its practice—fast, accurate, complete* — Wednesday, September 1, 1976

MD's Countersuit Challenges 'Shotgun' Malpractice Claims

Medical Tribune Report

CHICAGO—A countersuit has been filed by a Skokie (Ill.) physician against a lawyer to fight the alleged practice of naming physicians indiscriminately in malpractice suits when they have had little to do with the case.

Dr. Antone M. Pantone, a radiologist at Skokie Valley Community Hospital, has sued Chicago attorney James Thomas Demos for naming him as one of 20 defendants in connection with the 1972 death of a woman admitted to the hospital for childbirth.



DR. PANTONE

Dr. Pantone said his only connection with the case was supervising the routine chest x-ray required of everyone admitted to the hospital.

He is a colleague of Dr. Leonard Berlin of the radiology department who recently won a landmark jury verdict in a countersuit against two lawyers whom he had charged with legal negligence in failing to properly investigate the validity of a malpractice suit they filed against him (MT, July 7).

The Berlin verdict was hailed among the medical profession and in newspaper editorials as the beginning of a counteroffensive to blunt the rising tide of malpractice suits.

Joined in the countersuit by Dr. Pantone was Dr. Arnold B. Swerdlow, a surgeon at the hospital, who also was named as a defendant in the malpractice suit. Dr. Swerdlow said his only connection with the case was to answer a request made as he was walking down the hall to come to the patient's room and perform a venous

Continued on page 19

Dr. Cooper Acknowledges

Vaccine Trial Evaded Fed's Prisoner Ban

Medical Tribune Report

WASHINGTON, D.C.—Inmates in a Texas state prison have been used in tests of the new swine-type influenza vaccine even as the Federal Bureau of Prisons has banned the participation of federal prisoners in drug trials.

During an exclusive interview by Dr. Arthur M. Sackler, International Publisher of MEDICAL TRIBUNE, Dr. Theodore Cooper, Assistant Secretary for Health, Department of Health, Education and Welfare, said state prisoners represent "a minor part of our study population and were participating with full informed consent." He added that the prison clinical trials were conducted with recognition that the entire issue of prisoner participation was still being studied by a HEW panel on human experimentation.



DR. COOPER

"Full disclosure has indeed been made to volunteers in the clinical studies and will be required in the campaign for the general population," Dr. Cooper declared.

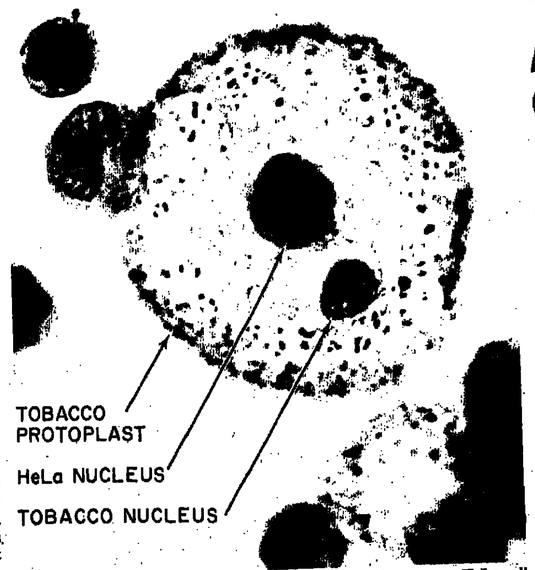
"Each of our study participants was required to sign an informed consent form," he maintained. The HEW official added that adequate information regarding the chances of an epidemic of the swine-type flu occurring, the extent of the danger, and the latest information on the safety and efficacy of the proposed flu vaccine, has been released to the general public.

Dr. Cooper said that the new vac-

Continued on page 20

Text of Interview, Page 13

First 'Interkingdom' Photomicrograph



First "interkingdom fusion" is shown in photomicrograph of human HeLa cell and tobacco hybrid protoplast after polyethylene glycol treatment. Picture from Brookhaven National Laboratory demonstrates HeLa nucleus inside tobacco cell and, at upper left, a HeLa cell adhering to protoplast surface.

Human-Plant Cell Fusion More Than Dramatic Lab Advance

By NATHAN HORWITZ
Medical Tribune Staff

NEW YORK—The first successful fusion of human and plant cells at Brookhaven National Laboratory—and concurrent reports of animal-plant cell fusions at other centers—has opened avenues of study that go well beyond a dramatic advance in laboratory technology, investigators here agreed.

The "interkingdom fusion" could give science a potent new genetic research tool, may have applications in cancer therapy and, ultimately, could lead to methods for giving protein cell cultures the capacity to grow by photosynthesis.

These were the views of experts who spoke with MEDICAL TRIBUNE in the wake of the news that the Brookhaven team had fused human HeLa cells with those of a hybrid tobacco plant, and that a team at Florida Atlantic Univer-

Continued on page 12

Pre-Angiogram Screen

Thallium May Allow Earlier CAD Diagnosis

Medical Tribune Report

DALLAS—Thallium^{201} imaging provides greater sensitivity and specificity than electrocardiography in determining suspected coronary artery disease Dr. Glen W. Hamilton, Veterans Administration Hospital, Seattle, reported here. Although the evidence is still preliminary, it appears that thallium imaging might permit earlier detection of coronary artery disease (CAD) and allow a more careful selection of patients who might benefit from angiography, he said.

The Seattle group was one of three medical teams that reported varying degrees of optimism on the potential of thallium imaging at a meeting of the Society of Nuclear Medicine held here.

The Seattle study included 71 patients, of whom 57 were shown to have CAD on previous electrocardiography, coronary arteriography and ventriculography, and 14 with no coronary artery disease.

Rest vs Exercise Studies

In rest studies, both ECG and thallium imaging revealed no CAD in the 14 patients, but exercise studies showed some false positives. "The ECG falsely predicted that 21% of the patients with no or insignificant amounts of CAD had ischemia when they didn't," said Dr. Hamilton. "The thallium imaging only falsely predicted one patient, or 7%," Dr. Hamilton stated.

In the 57 patients known to have CAD, 23% had ECG Q-waves showing prior infarcts during rest, while 40% had resting thallium defects. During exercise the ECG showed 56% of the patients with exertional ST depressions indicating ischemia, while 67% showed thallium perfusional defects.

Combined rest and exercise studies

Continued on page 12

INTERNATIONAL REPORT

from Germany *from the Editors of Medical Tribune Germany, Wiesbaden*

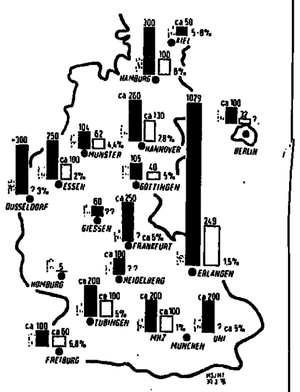
Germany Seen 'Underdeveloped' in Cardiovascular Surgery

Medical Tribune World Service

BAD NAUHEIM—German cardiosurgical departments and clinics are nearly all too small, too few surgical operations are performed in them, and the upward trend is all too dilatory. Operational requirements for acquired cardiovascular defects are only just covered, congenital heart defects are still not corrected with sufficient frequency, and in the field of cardiovascular surgery the Federal Republic is, bluntly, "an underdeveloped nation." These are the conclusions reached from the results of an inquiry through the German Society for Cardiac, Thoracic and Vascular Surgery, effected during the period 1970 through 1974.

Measured by the recommendations of American committees of experts, German cardiac surgery departments in 1974 were nearly all too small or only just reached the "minimal standard," on the basis of the frequency of operations using heart-lung machines. True, a distinct upward trend is evident from 1970 through 1974, but it is developing far too slowly. Out of 16 departments only three had had a frequency of operations exceeding 250 in 1970, three reached 250 per year, and the other 10 used cardiopulmonary bypass only occasionally, none of them reaching even 100 operations a year. These low efficiency departments were no longer so bad in 1974 but the bulk of the clinics (11) reached only 250; in six departments only was that figure exceeded in 1974. In nine out of 17 departments development is very slow, in two the frequency is even retrograde, and in the rest the situation is one of stagnancy. It is striking that one clinic with 674 operations in 1974, stands definitely and by a long way ahead, in the second, third and fourth places the numbers of operations announced were respectively 391, 344 and 321; all other departments stood below 300 per year.

Map shows 17 cities in Germany where cardiovascular surgery is now practiced. Heavy vertical bars indicate total number of such operations to date, light bars represent number last year. Percentage figure is proportion of premature deaths, and the year shows when cardiovascular surgery was first performed.



from Britain *from the Editors of Medical News-Tribune, London*

Most MDs Held Ill Equipped for Management of Weight Loss

Medical Tribune World Service

DUBLIN—The doctor's role in the treatment of obesity should be limited, says Professor Charles Hollenberg, Chairman of the Development of Medicine, University of Toronto.

He was speaking at the recent joint meeting of the British, Irish, and Canadian Medical Associations here.

Lack Special Knowledge

Most doctors, whether they be family doctors, hospital physicians or even endocrinologists do not have the time, the specialized knowledge or the interest to be successful in treating obesity, and they tend to approach the problem with a sense of "ordained failure," he said.

Professor Hollenberg feels that weight reduction should be mainly in the hands of an organized group of nutritionists, public health nurses and behavior therapists, while the doctor should limit his role to overseeing the general health of the patient at risk.

In particular, the doctor should be treating hypertension and hyperlipidemia in these patients rather than wait to see if these associations resolve spontaneously with successful weight loss.

Professor Hollenberg also discussed "new" information on several aspects of the medical treatment of obesity.

He said that certain principles have to be borne in mind irrespective of the kind of reducing diet prescribed.

A hypocaloric regime can lead to extensive loss of body protein as well as fat, and can induce ketosis which in turn can lead to hyperuricemia and bone catabolism.

A protein intake of 60 grams a day will reduce nitrogen loss to a minimum in a patient who is otherwise starving, while if 60-100 grams of carbohydrate are given as well, ketosis is practically abolished.

The 1,500 Calorie Diet

The commonly prescribed 1,500 calorie diet containing 100 grams of protein and 100 grams of carbohydrate allows for variety and individual choice while satisfying these requirements.

Also discussed by Professor Hollenberg was the potential of behavior modification therapy in which there is no attempt to uncover a psychological cause for overeating. The traditional psychiatric approach which tries to uncover hidden reasons for overeating have been unsuccessful. Behavior modification has only one goal in mind and that is to control overeating.

There have been reports of spectacular successes with this method at least in the short term, but long-term studies are required before proper evaluations can be made, said Professor Hollenberg.

from Japan *from the Editors of Medical Tribune Japan, Tokyo*

Beta-Blockers Lower Cardiac Output, Vascular Resistance

Medical Tribune World Service

SENDAI—Administration of various beta-blockers to essential hypertensive patients and those with high renin activity for determination of their possible effects on hemodynamics and plasma renin activity revealed that the hypotensive action of the agents was attributable to two factors: a decline in cardiac output; and a decline in peripheral vascular resistance. The extent of decline in blood pressure was correlated to the extent of decline in renin activity, the 73rd meeting of the Japanese Society of Internal Medicine was told by Prof. Yoshihiro Kaneko of the Department of Internal Medicine, Yokohama Municipal University.

Prof. Kaneko and his group initiated their investigation by studying hemodynamic effects of beta-blockers in a series of 61 outpatients with essential hypertension, including 41 males and 20 females with an average age of 42.4 years. In this study, seven drugs—propranolol, oxprenolol, carteolol, metoprolol, pindolol, bufetolol, and bunitrolol—were orally administered. In 35 cases whose blood pressure was lowered after four to five-week administration, pre- and post-treatment hemodynamics were determined by extra-corporeal measurement.

Different Mechanisms

Cardiac index was reduced in all groups except the pindolol group, whereas cardiac output showed either a downward trend or no significant change. There were three patterns of elevation, and no change or decline in peripheral vascular resistance. These findings were indicative of differences in hypotensive mechanism among different beta-blockers. Reduction in blood pressure occurred, the investigator noted, due to declined cardiac output in four drug groups involving propranolol, oxprenolol, carteolol and metoprolol, while it resulted from a decline in peripheral vascular resistance in the remaining three—bufetolol, bunitrolol, pindolol.

In delineating possible effects on plasma renin activity (PRA), 19 hypertensive inpatients with high-renin activity were given propranolol, oxprenolol, metoprolol, pindolol or bunitrolol orally for an average of 16 days. Radioimmunoassay showed that PRA declined in the propranolol, oxprenolol and metoprolol groups, but no significant changes were noted in the other groups.

Next Week

from France

The Editors of *La Tribune Médicale* will present an interview with Dr. Alexandre Minkowski, whose best-selling books have stirred considerable controversy over the delivery of health care in France.

index

CLINICAL NEWS NOTE: *"...the entire population is immunilogically vulnerable [to swine-type flu]. An epidemic would affect all age groups...We do not regard administration of the vaccine to the general population as an experiment. The vaccine will be fully licensed by the Bureau of Biologics of the Food and Drug Administration and will meet the same standards required of other vaccines....If there is any experiment involved here, it is one of logistics—to determine if we can successfully vaccinate essentially the entire population against a potential disease threat within a four-month period. The experience will be immensely valuable in developing effective disease prevention and control programs in other areas."* (Dr. Theodore Cooper. See page 13.)

Medicine **1, 3, 13, 23**

MD's countersuit challenges "shotgun" malpractice claims 1
Swine flue vaccine trial used state prisoners, evaded federal ban 1
Coronary artery disease detection may be hastened by pre-angiogram thallium imaging screen 1
Human-plant cell fusion seen as more than a dramatic lab advance 1
Cardiovascular disease: testosterone and estrogen both implicated 3
Death row inmates to receive special therapy 3
Text of interview with Dr. Cooper....13
Are physicians genetically programmed for self-destruction? 23

International Report: **2**

Obstetrics: **3**

Diuretics in normal pregnancy cited as "potentially hazardous" 3

feature index

Current Opinion 6
Book Biopsy 11
Editorials 11
Letters to Tribune 11
Editorial Capsules 12
Epigram 17
Medicine on Stamps 17
One Man ... and Medicine 17
Pediatric Progress 19
Clinical Trials 21
Immateria Medica 21

Medical Tribune

ARTHUR M. SACKLER, M.D.
International Publisher

Advisory Board
JOHN ADRIANI, M.D. • RENE J. DUBOS, Ph.D.
JULES H. MASSERMAN, M.D.
BERNARD LOWN, M.D.
ALTON OCHSNER, M.D. • LEO G. RIGLER, M.D.

HARRY HENDERSON, *Editor-in-Chief* — RICHARD GUBNER, M.D., *Associate Editor*
HAROLD POSNOT, *Executive News Editor* — NATHAN HOROWITZ, *Special News Editor*
JOHN H. HEWITT, *Associate News Editor*
WILLIAM PRIFTIS, *Art Supervisor* — LARRY LIPPMANN, *Picture Editor*

880 Third Avenue, New York, N.Y., 10022
Phone (212) 421-4000 • *Audited by Business Publications Audit of Circulation, Inc:* [redacted]

MEDICAL TRIBUNE *is published each Wednesday except on June 16, 30; July 14, 28; Aug. 11 25; Sept. 29; Dec. 1, 22, 29, by Medical Tribune, Inc., 880 Third Ave., New York, N.Y. 10022. Controlled circulation postage paid at Vineland, N.J. 08360 Subscription $50.00, Students $7.50.*

Testosterone and Estrogen Both Linked to Cardiovascular Disease

Medical Tribune Report

NEW YORK—Both testosterone and excessive levels of estrogen have been suggested as possible major risk factors for the development of cardiovascular disease and myocardial infarction in men, according to two separate recent reports.

Based on studies of the effect of testosterone, sex, and age on experimentally induced arterial thrombosis in animals, a Georgetown University physiologist believes that his results "provide for the first time significant experimental evidence for an association between sex and age and the development of thrombosis."

Moreover, anti-androgen diminished the effect of testosterone and lowered the mortality rate from thrombosis in male animals; estrogen administration also reduced thrombosis in males, Peter Ramwell, Ph.D., Professor of Physiology and Biophysics, explains, adding, "We hope these results may give impetus to further research for anti-androgens that would not feminize yet offer some form of protection to people against cardiovascular disease."

'Signs of Feminisation'

The role of hyperestrogenemia as a possible predisposing factor for myocardial infarction in men was examined by Dr. Gerald B. Phillips, Professor of Medicine at Columbia University College of Physicians and Surgeons. He found that seven of 15 men who suffered myocardial infarction between the ages of 32 and 42 had a "strikingly" slow rate of beard growth, three had evidence of gynecomastia, and three a loss of libido. All of the characteristics with the possible exception of gynecomas, predated the infection, Dr. Phillips reported in *Lancet* (July 3, 1976).

"The observation that signs of feminisation preceded the infarction suggests that the hyperestrogenemia also preceded the infarction and that hyperestrogenemia may be an important risk factor in myocardial infarction in men," Dr. Phillips stated. He noted that this possibility is supported by the NIH's Coronary Drug Project, which showed that men receiving estrogens daily over an 18-month period had an increased incidence of myocardial infarction.

"Although patients in the present

Continued on page 17

Obstetrician Cites Potential Danger Of Diuretics in Normal Pregnancy

Medical Tribune Report

DALLAS—The use of diuretic drugs during normal pregnancy—once a common practice but lately under attack—should indeed be considered "potentially hazardous," Dr. Ernest W. Page reported here at a meeting of the American College of Obstetricians and Gynecologists. Despite this finding, based on analysis of data on 17,138 pregnant women, many questions regarding the practice have not been conclusively settled, Dr. Page said.

"An unknown, but perhaps still considerable, number of physicians continue to prescribe diuretics during normal pregnancy," Dr. Page told MEDICAL TRIBUNE. While cautioning against their use for generalized edema during pregnancy, the New Jersey obstetrician emphasized that diuretics may still have a place in short-term therapy for grossly edematous pregnant women with hypertension.

Citing their study comparing perinatal mortality and delivery patterns in 4,035 women prescribed diuretics during pregnancy and 13,103 women not receiving diuretics, Dr. Page, who is Chairman of the Department of Obstetrics and Gynecology at New Jersey-Rutgers Medical School, and Ms. Roberta Christianson, of the School of Public Health, University of California, Berkeley, listed the following findings:

- The mean birth weight after each week of gestation was heavier for infants whose mothers received diuretics, regardless of whether the drug was prescribed early or late in pregnancy.
- The incidence of stillbirths and neonatal deaths (with gestation greater than 181 days) was higher in the diuretic mother group. Perinatal mortality among term births was 16% higher in mothers prescribed diuretics.
- A sizable excess of perinatal deaths occurred in the group prescribed diuretics near term.

Continued on page 20

Fla. Plans Therapy for Death Row Inmates

By MICHAEL HERRING
Medical Tribune Staff

STARKE, FLA.—Medical experience in treating terminally ill cancer patients has provided the basis for a program planned here by Florida State Prison officials to psychologically prepare death row inmates for the electric chair.

"What do you say to a man who is about to die at the hands of society?" asked prison psychologist Paul Dekker in a MEDICAL TRIBUNE interview.

Much can be learned, he believes, from physicians working with patients whose death is inevitable, particularly the work of Dr. Helen Keubler-Ross with hopeless cancer victims. He also noted that Florida is one of the first states to plan therapy programs for death row inmates since the Supreme Court recently upheld the constitutionality of the death sentence in five southern states.

The program is still in its early planning stages, partly because the court has extended a nationwide stay of execution following an appeal for individual consideration of each offender's case. However, Mr. Dekker said, prison officials have asked doctors and psychologists who have worked with dying cancer patients at Shands Teaching Hospital in Gainesville to treat death row inmates when the program goes into effect later.

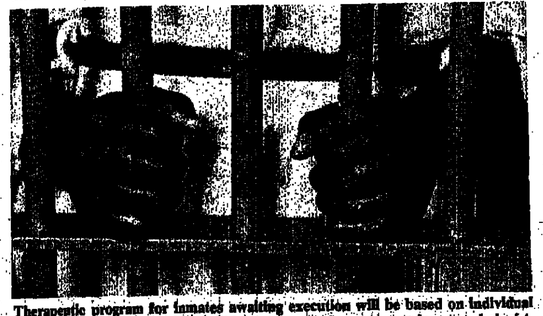
The plan is two-fold, with instruction for staff as well as therapy for the inmates. "Society may condemn a man to die, but he should still have the right to await his death—and die—with dignity. Capital punishment does not include torture," Mr. Dekker said.

Individual Crises

The medical experience in treating terminal cancer patients is "the closest thing we have to draw from, despite many basic differences. We want to establish a therapeutic program for dealing with each man's crisis individually," Mr. Dekker said. "As a result, we have no plans for an overall technique to treat the inmates involved."

The special training planned for prison employees is "to familiarize them with the situation we're all confronting when a man is about to be executed—the medical, psychological, and other aspects of the problem," Mr. Dekker said. He also noted that, because there have been no executions in Florida since 1964, a "whole new generation of staff workers have never seen or participated in an execution."

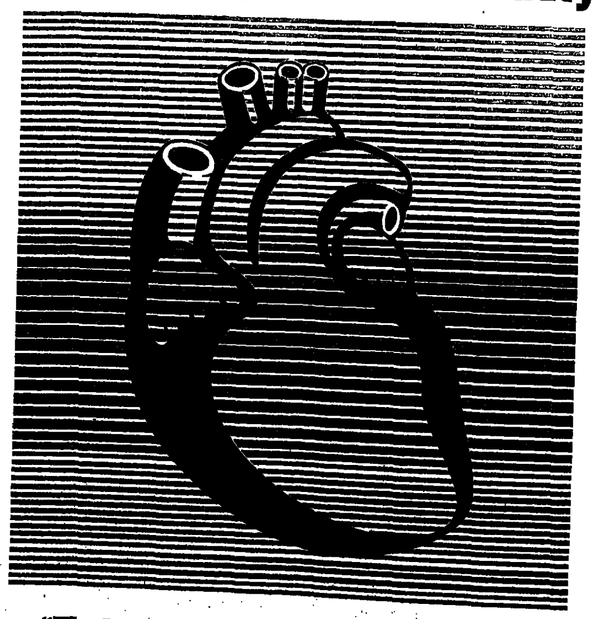
The application of medical and psychological research to prisoners on death row may seem bizarre at first, Mr. Dekker said. However, he regards it as "an open field where no scientific work has been done. The basic notion of offender rehabilitation is still punishment," he said, but the program, if not abolition of the death penalty itself, may serve to change that notion.



Therapeutic program for inmates awaiting execution will be based on individual needs and medical experience with terminal patients, says prison psychologist.

WHEN ANXIETY INTERFERES

The cardiac patient and anxiety



"The [cardiac] patient is anxious about minor symptoms, about the implications of his diagnosis, and about real or imagined limitations of function."*

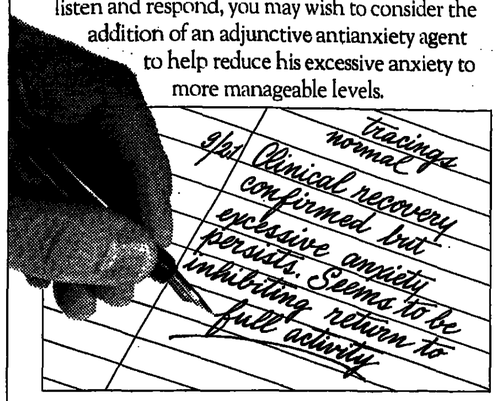
The worst is over. The cardiac patient is out of the acute stage, out of the hospital, and well on his way to recovery. How quickly he comes back to near normal functioning may depend on his psychological as well as his physical rehabilitation.

Clinical anxiety, for example, may be one reason for prolonged recuperation following cardiac healing. Yet anxiety can sometimes be beneficial in facilitating patient compliance.

The patient who is realistically concerned about resuming his precoronary functioning may be highly motivated to adhere to his rehabilitation regimen. However, the cardiac patient with *excessive* or unresolved anxiety may be so fearful of future heart failure that he refrains from your prescribed regimen.

Excessive anxiety can interfere with patient management

When excessive anxiety diminishes your patient's ability to participate fully in his rehabilitation program, your counseling and reassurance are often sufficient. But when his anxiety is so great that it actually interferes with his ability to listen and respond, you may wish to consider the addition of an adjunctive antianxiety agent to help reduce his excessive anxiety to more manageable levels.



Librium® (chlordiazepoxide HCl) an effective adjunct to your reassurance and counseling

Safety: Librium has a highly favorable benefits-to-risk ratio and a wide margin of safety. Because of its low incidence of side effects, it is regarded as one of the safest antianxiety agents available. And Librium does not adversely affect the cardiovascular system. See complete product information for warnings, precautions and adverse reactions.

Performance: Hundreds of clinical trials, thousands of published papers, and millions of patients constitute the record of performance for Librium.

Concomitant use: Of special significance in treating the cardiac patient already taking multiple agents is the fact that Librium is used concomitantly with most primary medications, such as cardiac glycosides, diuretics and antihypertensives.

*Zohman BL: *Geriatrics* 28:110-119, Feb 1973

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Adjunctive

LIBRIUM® IV

chlordiazepoxide HCl/Roche

5 mg, 10 mg, 25 mg capsules

THE ANXIETY-SPECIFIC

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager

Richmond Events Ltd
London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS

Tel: 081 332 2422

Information was correct at
to press 19th July 1994

Current Opinion

The Current Flu Controversy

By ARNOLD CHANIN, M.D.
Los Angeles, Calif.

THE CURRENT CRISIS generated by the possible occurrence of the 1918-A-Swine (New Jersey) influenza pandemic this fall and winter borders on the ridiculous. I cannot imagine what combination of factors has contributed to the government endorsed and sponsored program to innoculate the entire United States population, but we are ignoring many facts which may make this go down in history as another boondoggle. The effort will be expensive, may result in unnecessary illness from the vaccine itself, and is, ultimately, without real medical justification, no matter what big names are behind the program.

As we in medical practice know, the "flu" is not a killer. The "500,000" flu-related deaths in the United States during the 1918 epidemic were, as have been all flu-related deaths since, due to complications, mainly bronchopneumonia, viral pneumonia, and other forms of lower respiratory tract infection. As we also know, a patient who has multiple chronic diseases, such as chronic obstructive lung disease, congestive heart failure, diabetes, etc., is extremely vulnerable to secondary infection of any type. When these patients contract an influenza-like illness, it often tips the scales and throws them out of control. It is for this reason we as physicians have been giving such "high risk" patients annual influenza innoculations. Of course, we cannot always anticipate what influenza will strike our community, and thus the antigen-specific vaccines often are of little avail, as with this year's A-Victoria outbreak.

The Situation Today

It also must be emphatically pointed out that prior to the 1940s there were no antibiotics, and influenza complications, such as severe pneumonia, were difficult or impossible to treat effectively. If the patient did not have the strength to overcome the onslaught of influenza plus pneumonia, he/she could end up with a fatal illness. Younger individuals who pursue their normal activities despite cough and fever, rationalizing with "I just have the flu," are still in for difficult and often fatal respiratory infections. And now we have the further problem of heavy cigarette smoking, which makes the triad of chronic bronchitis, influenza, and bronchopneumonia especially deadly. But, looking at the total picture, now that we have not only the sulfas and penicillins, but even more effective antibiotics, flu-related deaths are not as prevalent as they were several generations ago.

The third factor in this current controversy is the fact that most children should not be given influenza injections. The American Academy of Pediatrics has never recommended immunizing children routinely. The cumulative effects of repeated flu injections (annually, of course, as the virus undergoes transformation) is not known and may not be known for decades. Therefore, many school children without chronic respiratory disease will be unnecessarily immunized against the 1918-A-N.J. virus.

Another aspect of this is that in 10 years of pediatric practice, I would estimate that over 90% of children brought into the office with "flu" either have severe bronchitis, bronchopneumonia, or lobar pneumonia. For some reason, influenza illness in the community, when transmitted to children, accelerates rapidly into lower respiratory tract infections.

Use of Amantadine

The fourth, and perhaps most significant factor, is that a drug developed in the early 1960s by Du Pont is available for both the prophylaxis and treatment of A-2 influenza. This drug, amantadine, gives approximately 80% protection when taken prophylactically, and about the same percent of effectiveness when given early in the course of influenza syndromes. It has been widely used all over the world, and in the United States since 1966. The Soviet Union has been using it for prophylaxis since the Hong Kong influenza pandemic of 1968-69, and it made headlines in many local newspapers. Russia not only has purchased over 10 million doses from Du Pont to use during the next flu season, it also is modifying the molecule in search of analogues, such as rimantadine.

The drug is administered in a small capsule, once or twice a day, and is virtually without side effects in most individuals. I use a dose of 100mg daily during the peak month or two of influenza in the community. For actual treatment of early, noncomplicated influenza, I use 100mg b.i.d. in adults and children over age 12, and 100mg daily in children under age 12.

Protection Against A-2 Variants

This drug, if taken by paramedical personnel, physicians, dentists, hospital staffs, would offer somewhere in the neighborhood of 80-85% protection against any of the A-2 variants which have come along in the past decade. And it must be noted that every significant influenza outbreak in recent years was an A-2 variant: Asian, Hong Kong, London, Port Chalmers, and A-Victoria. There is some early investigation which shows in vitro sensitivity to amantadine in the case of the 1918-A-N.J. strain, which, in all probability is a variant of the A-Victoria which also was evident in the Fort Dix population.

The concept behind the vaccines is that they must be antigen-specific, must anticipate the next year's influenza strain, and must be given prior to the actual outbreak of influenza in the community in order to be effective. The versatility of amantadine is that it can be given as soon as the outbreak hits the community (in this area of southern California the A-Victoria did not hit until February-March, 1976, because of the prolonged warm season in December-January); it can be given for several weeks or months, depending on the length and severity of the outbreak; and it can be used for treatment of uncomplicated A-2 influenza syndromes with remissinn of most symptoms within 48 hours.

Dr. Jonas Salk stated in an article in the *Los Angeles Times* that one reason to proceed with the immunization program is the fact that a 19-year-old Fort Dix recruit died from viral pneumonia. Dr. Salk's work in virology cannot be challenged, but we must scrutinize the death of this young man. First, he collapsed during a night march. Second, the A-1918-Swine virus was recovered from either blood or tissue. Third, the youth died from viral pneumonia.

Problem of Viral Pneumonia

The total picture here is not that influenza can kill, but that multiple factors, combined with flu, can cause morbidity and mortality. In this case the triad was: exhaustion from the march, influenzal infection, and viral pneumonia. There may have been other factors which, as yet, have not been revealed in the press. Certain questions would remain in the mind of any physician investigating such a death.

While we do not have a sure cure for viral pneumonia, supportive care and other modalities can often result in recovery when the patient is not overwhelmed with other disease entities. It might be well to point out, for the sake of further investigation, that in our local hospital, we used amantadine for treatment of viral pneumonia following the London flu outbreak of 1973/4. These patients failed to respond to various antibiotics, both as outpatients and in the hospital. Four cases responded to amantadine, including a father and son. I cannot draw any final conclusion here, and other areas of inquiry remain, such as treatment of viral pneumonia with amantadine plus antibiotics.

Attitude of CDC and FDA

Physicians have been reading about amantadine in the literature for many years, but have been reluctant to try it because of the lack of sufficient promotion by Du Pont and Endo (which now handles its distribution). We have the FDA and CDC to thank for that. The CDC is still telling American physicians to use "bed rest, aspirin, and fluids" for uncomplicated influenza. The media echo this refrain with every new flu outbreak. I wonder how many people die needlessly because they fail to seek medical attention solely because this wonderful advice is drummed into them annually. Some of these individuals are at home attempting to treat pneumonia with aspirin and fluids. By the time they do see their physician, they have severe respiratory disease, and many have to be hospitalized.

While Others Laugh

The FDA is still preventing any advertising of amantadine other than for the prophylaxis of A-2 (Asian) flu and in the treatment of Parkinson's disease and syndrome.

While Russia and other countries are laughing at our enthusiasm over the annual influenza immunization ritual, they go on using amantadine, rimantadine, and perhaps other effective antiviral agents in both the prophylaxis and treatment of the A-2 influenza syndromes.

WHEN CONSTIPATION IS CHRONIC
help change the pattern by facilitating regular elimination

Stimulate gentle peristalsis
With SENOKOT laxatives, regular comfortable evacuation was reported[2-11] in 93% of 529 cases of chronic constipation, including cases resistant to other therapy.

Dosage may be reduced gradually
Taken at bedtime, SENOKOT Tablets/Granules usually induce comfortable evacuation the next morning, gently and predictably. As regular elimination is established, dosage may be reduced gradually and eventually discontinued.
SENOKOT Tablets/Granules are virtually colon-specific[1] and generally free of side effects at proper dosage levels.

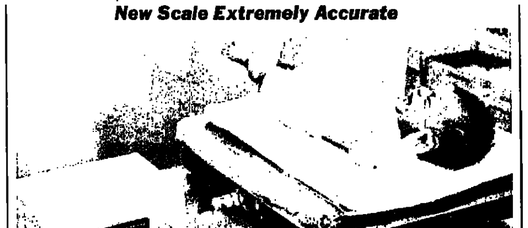
References: 1. Godding, E. W.: Therapeutic Agents, in *Management of Constipation*, edited by Sir Francis Avery Jones and Edmund W. Godding, Oxford, Blackwell Scientific Publications, 1972, p. 65. 2. Lowy, A.: *Int Rec Med* 173:803 (May) 1960. 3. Tirach, H., Rosenfeld, S.: *Am J Gastroenterol* 31:702 (June) 1959. 4. Peyton, T. R.: *J Natl Med Assoc* 49:388 (Nov.) 1957. 5. Lemphier, T. A., Ehrlich, R.: *Am J Gastroenterol* 27:381 (April) 1957. 6. Flinlen, P., Weeden, G. D.: *Lancet* 1:497 (March 7) 1953. 7. Sarles, H., Camatte, R.: *Provence Med* 38:3 (Dec.) 1970. 8. Heward, L. R. C.: *Acta Gastroenterol Belg* 29:810, 1966. 9. Blanc, Choux, J.: *Bud Med & Chirurg* No. 2466 (Nov. 30) 1964. 10. Baujat, J. P.: *Gaz Hopitaux* 136:465 (April) 1964. 11. Rousseau, G., *et al.*: *l'Ouest-Med* 16:129 (Feb. 10) 1963.

Purdue Frederick
© COPYRIGHT 1976 THE PURDUE FREDERICK COMPANY/NORWALK CONN. 06856

SENOKOT® tablets granules
(standardized senna concentrate)
Senokot laxative claims are documented
a natural vegetable laxative



New Scale Extremely Accurate



Accurate to within 1/100 of a pound, the electronic scale above, invented by M.I.T. researcher James Williams, can detect minute changes in body weight essential to clinical studies of body composition and protein utilization.

You Know Medicine



He Knows Money

Are your personal investments performing up to your expectations?
What about your professional corporation?

Internationally-respected financial analyst and economist *Eliot Janeway* has recently spoken at a number of regional seminars directed to the specific financial and investment problems doctors are up against. The response has been overwhelming.

Janeway's combination of political savvy, economic astuteness and financial expertise offers physicians the chance to put their business affairs on a sound and practical basis, with answers to questions like these:

- **How can you get the highest possible return on an investment without locking your money up?**
- **How can you maximize income and protect capital in your pension fund?**
- **What's in sight for stocks, bonds, interest rates, gold, foreign deposits?**
- **What's the future of owning land in America?**

Only an expert who lives with the world of money and politics every day can answer these questions. Eliot Janeway does. It every week in *THE JANEWAY LETTER.*

Consult Eliot Janeway's Letter. Get behind the news and ahead of the trends. Get your investment planning on a track that will work for you and pay off in the years to come.

The Janeway Letter
15 E. 80th Street, NYC 10021

Name _____
Address _____
City _____ **State** _____ **Zip** _____

☐ *I enclose $5 for 2-week trial.*
I prefer The Janeway Letter for
☐ *3 mo.($40)*
☐ *1 yr($125)*

Next full-day Janeway seminar, New York, September 30. Check to receive information. ☐

Special Offer — Personally Autographed Janeway's classic history of the government's role in inflation ECONOMICS OF CRISIS. $7.50 (list $10) ☐

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager

Richmond Events Ltd
London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS

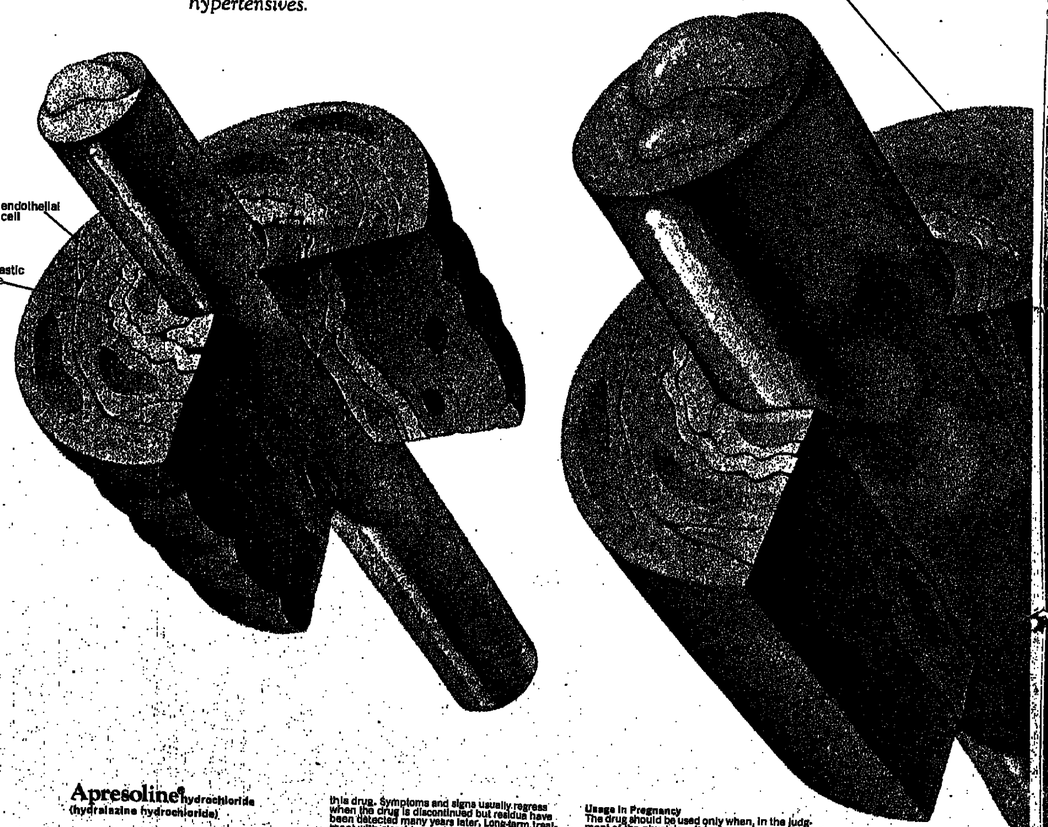
Tel: 081 332 2422

Information was correct at t
to press 19th July 1994

Apresoline®... (hydralazine) relaxes arterioles to hemodynamic solve the major problem in hypertension

Abnormally high peripheral resistance is the major hemodynamic problem with most hypertensives.

Apresoline reduces peripheral resistance and lowers blood pressure through a direct relaxation of arteriolar smooth muscle.



high peripheral resistance: common attribute of most hypertensives

Because high peripheral resistance is the major hemodynamic disturbance found in most patients with essential hypertension,[1,2] the therapeutic goal should be reduction of total peripheral resistance and a return to more normal peripheral circulation.[1,2]

Hence, vasodilating drugs "...offer a physiologically rational approach to the therapy of hypertension."[1] In addition, "...vasodilators [combined with a sympathetic inhibitor] are the most predictable and specific drugs for reversing the hemodynamic abnormality of most hypertensive patients."[1,3]

the only oral agent that deals directly with this problem

Apresoline (hydralazine), the only currently approved oral antihypertensive with vasodilating action, decreases peripheral resistance—regardless of its cause—and, hence, arterial pressure by relaxing arteriolar smooth muscle. Accompanying the fall in blood pressure is a rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

a different and complementary pharmacologic approach

Different in action from all other oral antihypertensives and compatible with most of them, Apresoline can play a significant role in a variety of therapeutic combinations.

Such combinations, according to Freis,[4] with each component representing a different antihypertensive mechanism, provide the most effective way to control blood pressure. This approach may also permit lower drug dosages.

the problem of postural hypotension minimized

Nickerson[5] describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Continued on following page

Apresoline® hydrochloride
(hydralazine hydrochloride)

TABLETS

INDICATIONS
Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS
Hydralazine may produce in a few patients a clinical picture simulating systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary.

Complete blood counts, L.E. cell preparations and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

Usage in Pregnancy
The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS
Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent:* Nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.

DOSAGE
Initiate therapy in gradually increasing dosages; adjust according to individual response. Start with 10 mg 4 times daily for the first 2 to 4 days. Increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level.

The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline.

In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a thiazide, reserpine, or both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

HOW SUPPLIED
Tablets, 10 mg (pale yellow, dry-coated); bottles of 50, 60, 100 and 1000.
Tablets, 25 mg (deep blue, dry-coated) and 50 mg (lilac, dry-coated); bottles of 30, 60, 100, 500 and 1000.
Tablets, 100 mg (peach, dry-coated); bottles of 100.
Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

CIBA

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager

Richmond Events Ltd
London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS

Tel: 081 332 2422

Information was correct at
to press 19th July 1994

Apresoline® (hydralazine) ...key component in the "guideline" antihypertensive regimens

AMA Committee on Hypertension Recommendations

Table 1.—Regimens for the Management of Uncomplicated Hypertension

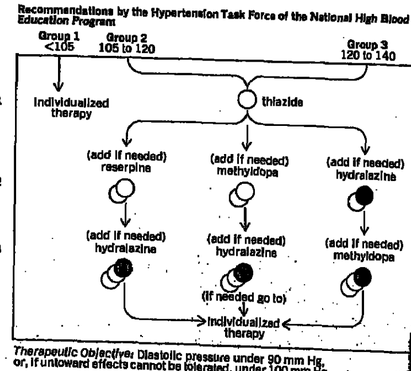
	Alternative 1	Alternative 2	Alternative 3*	Alternative 4
Initial therapy	Thiazide diuretic	Thiazide diuretic	Thiazide and guanethidine	Thiazide diuretic
Add, if necessary	Methyldopa	Reserpine	Methyldopa and hydralazine or both	Propranolol (unlabeled use)
	Hydralazine	Hydralazine		Hydralazine

*In patients who cannot tolerate guanethidine, alternatives 1 or 4 may be given a therapeutic trial, but treatment should be initiated with *both* the diuretic and methyldopa or propranolol.

(Adapted[6])

Apresoline... included in all four treatment plans by the AMA Committee[6]

Recommendations by the Hypertension Task Force of the National High Blood Pressure Education Program



Therapeutic Objective: Diastolic pressure under 90 mm Hg, or, if untoward effects cannot be tolerated, under 100 mm Hg.

(Adapted[7])

Apresoline... recommended second and third step therapy by the Hypertension Task Force[7]

used effectively in the landmark VA studies[8,9]

Apresoline was one of the three basic drugs used in two published VA cooperative studies—studies which demonstrated conclusively the benefits of antihypertensive treatment in reducing risk of morbidity and mortality.

Apresoline®... (hydralazine) An antihypertensive idea whose time has come



References
1. McNay JL: Adrenolytic and vasodilator therapy. *Postgrad Med* 56:76-80, 1974.
2. Koch-Weser J: Vasodilator drugs in the treatment of hypertension. *Arch Intern Med* 133:1017-1027, 1974.
3. Koch-Weser J: The vasodilator antihypertensives. *Drug Therapy* 5:57-61, 1975.
4. Freis ED: Hypertension: A controllable disease. *Clin Pharmacol Ther* 13:627-632, 1972.
5. Nickerson M: Antihypertensive agents and the drug therapy of hypertension, In Goodman LS, Gilman A (eds): *The Pharmacological Basis of Therapeutics*, ed 4. New York, The Macmillan Company, 1970, p 729.
6. Committee on Hypertension: Drug treatment of ambulatory patients with hypertension. *JAMA* 228:1647-1655, 1973.
7. Report of Task Force I, National High Blood Pressure Education Program: Recommendations for a National High Blood Pressure Program Data Base for Effective Antihypertensive Therapy, Sept 1, 1973, DHEW Publication No. (NIH) 74-529.
8. Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967.
9. Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1182, 1970.

CIBA

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News

Published by Medical Tribune, Inc.

A Measure of Thrombosis Risk

LANCET'S RECENT EDITORIAL, "Antithrombin" (*June 19*) reports a promising direction in the "dogged search for a reliable and simple test for the early detection of a tendency to thrombosis." The editorial focuses on the studies of Innerfield in which a low serum antithrombin has been found to characterize patients with both venous and arterial thrombotic disorders, i.e., deep-vein thrombosis, and arteriographically proven advanced occlusive coronary artery disease (*Scand. J. Haemat.* 16:202, 1976, and *Am. J. Clin. Path.* 65:64, 1976).

In addition, there is significant evidence from prospective studies that low antithrombin activity is a harbinger of thrombotic complications in individuals and circumstances predisposing to thrombosis, e.g., surgery in women taking contraceptive pills and older persons undergoing total hip replacement surgery (S. Sagar et al., *Lancet* 1:509, 1151, 1976).

Antithrombin activity is dramatically enhanced by heparin. This action has been employed by Innerfield in modifying the assay of antithrombin activity. The heparin antithrombin assay involves the determination of the prolongation of clotting, when standardized thrombin and fibrinogen solutions are mixed, by the addition of aliquots serum and heparin.

The co-action of antithrombin and heparin has therapeutic implications, now so thoroughly proven as to constitute therapeutic indications, if not indeed injunctions. Anti clotting activity is greatly enhanced by mini-doses of heparin, and heparin in small subcutaneous doses of 5000 units twice daily has proven of great value clinically in preventing thrombosis. Introduced in 1962 by Sharnoff, the utility of the regimen to prevent deep vein thrombosis has been documented by Kakkar, Wessler and many other investigators.

Particularly important is the documentation of efficacy in an international multicenter trial of the prevention of fatal postoperative pulmonary embolism by low doses of heparin (*Lancet* 2:45, 1975). The evidence points strongly to a low concentration of antithrombin as cause for a hypercoagulable state postoperatively, and prevention of operative fall in antithrombin activity by a small dose of subcutaneous heparin, thereby reducing postoperative thrombosis (S. Sagar et al., *Lancet* 1:509, 1976).

Low serum heparin antithrombin activity provides a simple and useful test to indicate predisposition to thrombosis. It ought to be employed routinely preoperatively to identify likely candidates for postoperative thrombosis. A low serum antithrombin level also appears to be a significant risk factor in addition to those which are well identified for coronary and stroke candidates. Whether reduction in morbidity and mortality from coronary and cerebral arterial thrombotic vascular disease can be achieved by agents such as platelet anti-aggregants, e.g., aspirin, remains to be proven, but in the case of prevention of venous thrombosis and pulmonary embolism the evidence is clear. R.S.G.

Confusion Worse Confounded

THE ROUND-UP ON PAGE 3 of experience with androgens and estrogens leaves the poor clinician at a loss. Professor Peter Ramwell at Georgetown University reports that androgens increase the development of arterial thrombosis while estrogens and antiandrogens generally reduce it. Meanwhile, Dr. Gerald B. Phillips at Columbia finds that increased estrogen levels in young males seem to be associated with a tendency to myocardial infarction—i.e., estrogens promote arterial thrombosis. Dr. Ramwell is reported as saying that "there is no conflict" between his findings and those of Dr. Phillips. Maybe so, but the makers of oral contraceptives must include a warning about thrombotic, thromboembolic and cerebrovascular disease and myocardial infarction as well. And a long-term study of several medications in the treatment of patients with coronary artery disease early on abandoned the use of estrogens because of untoward effects.

The Current Flu Controversy

CLINICAL QUOTE: "THE CURRENT CRISIS *generated by the possible occurrence of the 1918-A-Swine (New Jersey) influenza pandemic this fall and winter borders on the ridiculous. I cannot imagine what combination of factors has contributed to the government endorsed and sponsored program to immunize the entire United States population, but we are ignoring many facts which may make this go down in history as another boondoggle. The effort will be expensive, may result in unnecessary illness from the vaccine itself, and is, ultimately, without real medical justification, no matter what big names are behind the program.*" (Dr. Arnold Chasin, of Los Angeles, Calif. See *Current Opinion*, page 6.)



"Let me remind you, Madam, this is not a talk show..."

© 1976, Medical Tribune, Inc.

LETTERS TO TRIBUNE

On the Canaanites

I enjoyed the "One Man... and Medicine" article on the Canaanites (MT, May 26). My sources indicate that "Canaan" is understood to mean belonging to and in the land of purple; that the most chacteristic Canaanite occupation was trading, purple dye in particular. In the Old Testament, "Canaanite" is used to denote a trader or merchant.

The Greek name, "Phonecia," refers to the purple industry also. Close similarities between the Hebrew and Phoenician scripts have been described.

The Canaanite social structure consisted of several strata: freemen, semi-freemen, and slaves. Their economy was based on agriculture. Land could be privately owned, or possessions of the temples or state. The nation was poor and marked differences in living standards betweeen the patricians and the wide range of lower class people such as the half-free, serf, an slaves, is proven by the excavation of both fine houses as well as crude ones. Guilds were wide-spread throughout Canaanite society among farmers, artisans, traders, priests, musicians and warriors.

The Canaanite religion gives hints of an extensive pantheon. The diety El was its senior. Baal was the most significant god. Some of the inhabitants of Israel were attracted to the Canaanite lifestyle because it lacked the rigidity and ethical demands of the faith of Israel. It was the task of the prophets to draw the defining line between the worship of Baal and the worship of Yahweh. A challenge of Elijah on Mt. Carmel, "If Yahweh is God, follow him; but if Baal, then follow him," summarizes in succinct form the problem that the prophets faced for the span of many centuries.

CLAUDE A. FRAZIER, M.D., P.A.
Asheville, N.C.

After the Dam Collapsed

Now that the Teton dam has collapsed, causing countless damage and numerous deaths, plus ensuing uncountable episodes of illness due to infection, stress and "mental suffering," I wonder if the engineers and architects, contractors and electricians will join the unfortunate ranks of the doctors, having to renew their licenses, explain their motives, and keep records of their personal relation to every brick and pound of mortar...

EVA LEE SNEAD, M.D.
San Antonio, Tex.

Correction

Inadvertently, a transposition in the attribution following Dr. Charles Harris' name occurred in the August 4 issue. The initials appeared as F.A.C.P. when they should have appeared as F.C.A.P.

Book Biopsy

Hematology—Physiologic, Pathophysiologic and Clinical Principles, *by James W. Linman, M.D., Macmillan, New York, 1975, $34.95.*

From the Preface:

"This book has been written for medical practitioners in specialties other than hematology... a clinically oriented book and has as its ultimate objective the presentation of information concerning the diagnosis and treatment of all types of hematologic disorders, both primary and secondary. Basic clinical observations (the history, physical findings, and routine hematologic studies) are emphasized throughout, and an attempt is made to place newer and more complicated techniques in proper perspective. However, an understanding of the pathophysiology of disease is a requisite for accurate diagnosis and proper treatment, and the discussion of each hematologic disorder is preceded by detailed accounts of the pertinent physiology. For example, the chapter dealing with iron metabolism begins with a consideration of normal iron metabolism, the section on hemorrhagic disorders with a description of the normal coagulation mechanism, the chapter on myeloma with a discussion of immunoglobulins, and so on....

"All readers will obviously not find every portion of this book to be 'tailor-made' for their interests level of training, or experience. For example, the busy clinician who is seeking current information concerning the diagnosis and treatment of pernicious anemia may not have the time or the inclination to master the intricacies of the biochemistry of the cobamide or folate coenzymes. Thus, certain sections have been designed to stand alone (e.g., the discussions of clinical manifestations do not demand a prior reading of the portions devoted to pathophysiology)...."

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager

Richmond Events Ltd
London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS

Tel: 081 332 2422

Information was correct at

Human and Plant Cell Fusion May Offer New Ca Therapy

Continued from page 1

sity had fused hen red blood cells with those of the tobacco hybrid.

Harold H. Smith, Ph.D., Senior Geneticist at Brookhaven and head of the team that produced the human-plant cell fusion, said that a Hungarian group also, recently, fused human blood cells with those of a carrot strain.

Dr. Smith said the key to the interkingdom fusion at his laboratory was the use of polyethylene glycol (PEG), a synthetic compound that appears to alter the electric charge of both plant and animal cells and helps to make them adhere to each other. In the study, the cells of a tumor-prone tobacco hybrid were stripped of their walls by enzyme digestion and then placed, with HeLa cells, in a medium containing PEG.

'Strategy' Outlined

The "strategy," said Dr. Smith, was to use the plant protoplasts as recipient carriers of the HeLa cells. Within one hour, a number of HeLa cells were attached to the protoplasts and, within three hours, some tobacco cells were seen to contain single HeLa nuclei. The observations were continued for four to six days, with increasing numbers of fusions taking place.

To make certain that the HeLa nuclei had actually been incorporated into the tobacco cells and were not simply superimposed on their exterior—a possible mistake in optical microscope observations—the team labeled the HeLa cells with radioactive tritium and demonstrated incorporation by autoradiographs. The HeLa nuclei, Dr. Smith reported, retained their integrity for six days.

In an inteview, he said that an immediate line of research suggested by the study would be gene investigation. "Since human and tobacco genomes are so different, we can identify the genes associated with particular human chromosomes by their characteristic proteins and isoenzymes in the plant protoplast." The technique would increase the number of identifiable genes and would help to locate them more precisely on the chromosome, Dr. Smith noted.

Since the publication of the original report in *Science* (July 30), Dr. Smith said, his team has done two additional studies. One was undertaken to see if HeLa cells will grow in a medium similar to that used in culturing plant cells. "We were surprised to find that HeLa cells can grow in a mixture of 70% HeLa medium and 30% calf plant medium. The plant medium does not contain fetal calf serum, considered essential for HeLa growth, and the HeLa medium lacks plant hormones." In the second study, the team has maintained and grown interkingdom protoplasts in an environment "in which cell colonies can be expected to develop. We haven't as yet been able to determine if the protoplasts contain human chromosomes, but they have grown for eight days and should grow indefinitely."

In the Florida studies of hen blood cell-tobacco cell fusions, the team employed procedures similar to those in the Brookhaven studies, according to James X. Hartmann, Ph.D., Associate Professor of Microbiology. Dr. Hartmann told MEDICAL TRIBUNE he had chosen red blood cells for the experiment because the vivid color difference between these and the green plant cells made it easier to identify the respective components under the light microscope. Additionally, the hen erythrocyte nucleus provides an easy marker, he noted.

Toward The Future

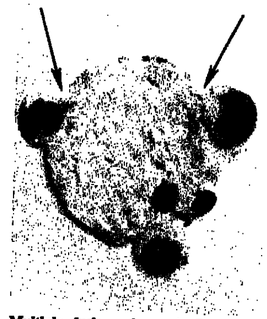
Commenting on the possible applications of these studies, Dr. Hartmann stressed he was talking "very much in the future tense," but said that he could forsee a medical role for the interkingdom cells as subcellular membrane sacs —"mini-cells"—that could package cytotoxic drugs for use in cancer therapy. In this concept, cancer cells would be obtained from a patient, fused with a plant protoplast and reintroduced into the patient as a drug-carrying package. The advantage of using the patient's own tumor cells, Dr. Hartmann noted, is that they would increase the package's "recognizeability" and would thus be taken up selectively by the tumor. The plant component would facilitate penetration of the tumor cells.

Along more "blue-sky" lines of speculation, he suggested that it may be possible to use photosynthesis to "grow" the animal component of interkingdom cells, thus raising the prospect of culturing animal protein by sunlight alone.

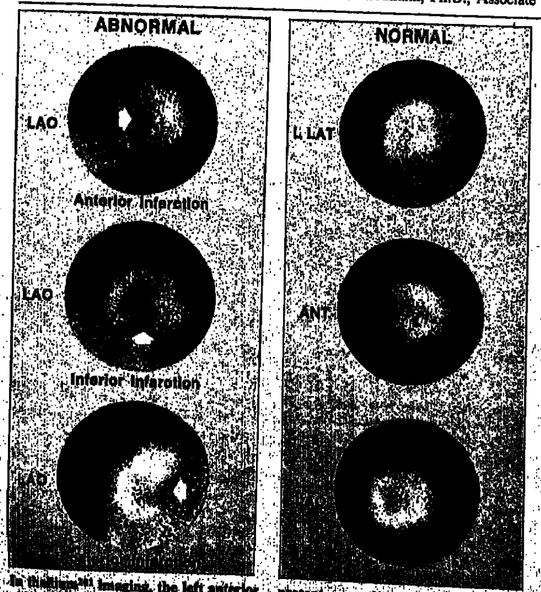
The National Aeronautics and Space Administration has already shown interest in this phase of the Florida studies, he said. "It is very feasible to expect that at the cellular level we can introduce photosynthesis into animal cells that we culture," Dr. Hartmann stated.

At NASA headquarters in Houston, Michael Lowenstein, Ph.D., a visiting scientist who is studying photosynthesis for its possible applications in developing food sources for space stations, confirmed that he has been in touch with the Florida microbiologist.

"Although Dr. Hartmann's team has not yet succeeded in growing animal cellular protein by photosynthesis," he declared, "the studies represent a remarkable development and have opened up some interesting lines of thought."



Multiple fusion of two HeLa nuclei with a tobacco cell is shown in this photomicrograph taken by Dr. Hnrold H. Smith's team at Brookhaven. Note the continuity of the membranes (arrows) 18 hours after fusion has taken place. In next phase of the investigation, the team plans electron microscopic studies of these interkingdom structures.



In thallium-201 imaging, the left anterior oblique (LAO) views, shown on left, best differentiate major coronary arterial beds; myocardial image defects present on resting study generally represent myocardial infarction. Normal thallium-201 images, on right, are shown in three standard views.

Thallium^{201} Imaging Aids Dx Of Coronary Artery Disease

Continued from page 1

showed ECG was able to detect 65% of the CAD patients and thallium 81%. Together, the techniques detected 90% of patients with CAD, Dr. Hamilton declared.

A similar study done at the University of California, San Francisco, showed that in a group of 34 patients evaluated for CAD, 16 had "equivocal treadmill ECGs," Dr. David Shames reported. Of the 16 patients, 10 were positive for CAD on both thallium imaging and arteriography. Six were negative on imaging, four having negative and two positive arteriograms.

"Thus, 14 of 16 patients, or 88%, were correctly identified by thallium imaging," Dr. Shames noted.

"Stress induced defects on ECG are difficult to interpret," he told MEDICAL TRIBUNE. "We termed an ECG 'equivocal' for CAD if the ST segment was abnormal at rest (such as may be found in left bundle-branch block, left ventricular hypertrophy, digitalis and other conditions) or if the ST segment showed significant, yet nondiagnostic, stress induced ST segment depressions."

Dr. Shames concluded that thallium^{201} appears to be not only more sensitive but more specific than ECG alone. "The use of thallium in detecting heart disease in patients with atypical chest pain is here to stay," he said.

"Today as many as 25% of the patients undergoing angiograms are negative for CAD," he added. "If we could exclude these patients ahead of time, it would reduce morbidity and mortality."

However, a Johns Hopkins researcher was not quite as optimistic. Dr. Ian Bailey reported on a Hopkins study that included 63 patients with angiographically proven CAD. Thallium imaging was better than ECG in the detection of one vessel disease, but in two and three vessel disease the differences between the two techniques were insignificant, Dr. Bailey said.

He warned that the presence of significant coronary artery disease couldn't be excluded when both techniques were negative.

A total of 83% of the patients with CAD were detected by ECG or thallium imaging, leaving about 17% undetected. "When both methods are used together, there is pretty good evidence of no coronary artery disease, but it's not absolute," he said.

According to Dr. Hamilton, a cooperative study among five institutions is being formed, and more data should be forthcoming soon.

Text of Interview: Part III

Dr. Cooper: Swine Flu Shots For All Not 'An Experiment'

You have indicated that there has been no "evidence of increased cancer or birth defects as a result of influenza pandemics." Isn't it true that it is only recently we have become sensitive to teratogenic effects of environmental pollutants and viruses? Could not the observations on past pandemics have missed a potential causal relationship?

Certainly, no surveillance system is ever perfect. But one would think that if the influenza virus had some teratogenic capability, that there would have been an increase in defective babies born following major flu epidemics infecting millions of persons. To our knowledge there has not been.

Is it not true that the government's requirement for "substantial" efficacy for drugs is not applicable to the swine flu vaccine?

Our past experience indicates that influenza vaccines are up to 90% effective when the virus used to make the vaccine matches that which is circulating in the community. The new swine-type vaccine has displayed similar results in adults. We are still compiling the data for children.

Can double-blind studies be done with the vaccine to meet the standard FDA type drug clearance requirement?

I am not certain what circumstances you are referring to. However, a double-blind protocol was employed in the clinical trials. The purpose is to get objective data on the incidence of side effects, which are usually minor but quite subjective in their severity.

What about dosage levels?

These levels are being determined from the clinical trial data, but it appears that all doses tested produced an effective antibody response in adults. We are continuing our studies in children to determine an effective dosage that will produce minimal side effects.

Will prisoners participate in the screening program? How does this compare with recent recommendations that such individuals cannot volunteer to participate in drug research?

Inmates of a state prison in Texas are participating with full informed consent, although prisoners comprise a minor part of our study population. HEW has never said that prisoners should not participate in drug trials, although the issue is under consideration by the Secretary's panel on human experimentation. The Federal Bureau of Prisons, however, has ruled that federal prisoners are not to participate in clinical studies. All prisons will be offered the vaccine when it is generally available.

Has full disclosure been made to both volunteers and the general public both as to the chances of the epidemic occurring, the extent of its dangers, or the efficacy and potential side effects of the vaccine?

Full disclosure has indeed been made to volunteers in the clinical studies and will be required in the campaign for the general population. Each of our study participants was required to sign an informed consent form. I believe we have given the public full information about the chances of an epidemic occurring, the extent of the potential danger, and most up to date information we have on the safety and efficacy of the vaccine.

But we have also emphasized the fact that this program is prudent disease prevention. We have stressed that we took the action we did because of the possibility of a serious epidemic, not because of its probability. We were able to act because for the first time we have enough advanced warning and lead time. We believe we have the technology to produce substantial quantities of quality vaccine, and we have the capability to administer it through state and local heatlh departments, and private physicians and health care facilities.

Will the government obtain signed "informed consent" releases from each person who is vaccinated?

State and local health departments will obtain signed "informed consent" releases from persons getting their shots from a public health clinic, even though the vaccine will be properly licensed and not considered experimental. Informed consent is not routinely required for either licensed biologics or new drugs.

What is the morality of vaccinating *every* person in a population to prevent a pandemic whose potential threat would be primarily to the elderly and high risk groups?

The swine-type virus has not been observed in person-to-person transmission since before 1930. Therefore, the entire population is immunologically vulnerable. An epidemic would affect all age groups. While the incidence of life-threatening complications would probably not be as high among young people as among the elderly and chronically ill, the actual numbers of complicated cases would be sufficiently high in an epidemic situation to warrant immunization of all persons who are medically able to take the vaccine. We will set the minimum age for participation by children after the final clinical trial data are reviewed.

Can one accept the entire population of the United States as part of an experiment either as recipients of the vaccine or as controls?

We do not regard administration of the vaccine to the general population as an experiment. The vaccine will be fully licensed by the Bureau of Biologics of the Food and Drug Administration and will meet the same standards required of other vaccines.

If there is any experiment involved here, it is one of logistics—to determine if we can successfully vaccinate essentially the entire population against a potential disease threat within a four-month period. The experience will be immensely valuable in developing effective disease prevention and control programs in other areas.

What about the "long-term follow-up" currently under consideration for other experimental medications? In view of the scope and the unanswered questions indicated above, what plans have been made for such monitoring of this unique national experiment?

We do not plan any long-term follow-up of the general population participating in this program except through normal public health disease surveillance activities. Children participating in the clinical trials will be followed for several years because of the opportunity we have to expand our knowledge of the long-term effects of influenza vaccines in this age group, which in the past has not been a significant recipient of influenza vaccine. We feel that we have gained a great deal of long-term experience with influenza vaccines over the past 30 years of their use, including a period in the 1950s when a strain of swine virus was included in a "broad spectrum" influenza vaccine used in an attempt to anticipate circulating virus strains.

Can you advise as to the considerations given to the immunization of pregnant women with swine flu vaccine?

Our advisory committee on immunization practices has already recommended that pregnant women receive the vaccine.

And what about drug and malpractice liability? Should not funds be made available to protect individual patients from even isolated disastrous consequences, such as occurred with the earlier polio vaccines? In addition to patient protection, should not physicians be protected against malpractice liability by suitable legislation in the projected national undertaking?

As I said before, liability has been very much an issue in the development of this program. Because of the Reyes v. Wyeth case, companies have sought total indemnification except, of course, for demonstrated negligence on their part in the manufacture of vaccine. And we have requested the authority from Congress to provide it.

It is our impression that there was relatively little public discussion prior to the making of the decision either in government hearings or detailed press coverage.

I must disagree with you about the degree to which these issues have been explored in the public press. Press coverage has been extensive. I have personally appeared on all three morning network shows to answer questions about the vaccine and the program, and to debate critics of the program. Our scientific meetings have been held publicly and we have encouraged press coverage. Most of the public comment we have received has been favorable. Some has been critical and an even smaller percentage opposed. We plan to continue this discussion of the issues through the media, including both the public and the trade press, and I invite your help in this regard.

It appears to me from the above that the government is following a double standard in the influenza vaccine program. Would you not agree that vaccines are being treated differently than drugs and that scientific theory and expertise rather than available hard data are the basis of decision making in this instance?

You suggest we are following a double standard in the influenza immunization program. I disagree.

We will license this vaccine according to the same standards imposed on other similar vaccines. No standards will be relaxed for the sake of expediency. Furthermore, the decision to launch this program was not made solely by federal officials.

From the beginning, we consulted with dozens of experts on influenza and vaccines about the significance of the findings at Fort Dix and the course of action which that finding suggested. In fact, even the President did not announce his decision to accept our recommendation for a national program without first personally asking 30 experts for their consensus, at a meeting held at the White House.

EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

Ca: Reaction to a Cause

". . . There is, we believe, no question that we have entered an era in which major causes of other human cancers will shortly be revealed. All the facts point to the likelihood that these causes will be chemical, although doubtless many secondary factors will play important roles. More research is urgently needed in this field in the universities and medical schools. The practicing physician is in a position to make major contributions by merely looking at each cancer case he sees from the standpoint of a reaction to a probable cause and asking questions pertinent to this possibility. The possible introduction of new carcinogenic agents anywhere in our complicated existences must be guarded against, but we must not let extremism take charge and jeopardize the reasoned objectivity that has led us forward to where we can at last envision a control of cancer." *(Editorial, P. Shubik, D.M., D. Phil.; and David B. Clayson, Ph.D., Ann. Int. Med. 85:121, July, 1976)*

Boring Medical Education?

". . . good listening means being open and flexible to all relevant changes in a given situation. It means giving your speaker the chance to present all his facts and ideas before jumping to premature conclusions or reacting emotionally. . . .

"In summary, listening is a very live and active process. It demands much more than remaining quiet so the other person can have his say. It involves active participation, discipline, concentration, patience, freedom from distraction, and openmindedness. There is little opportunity for boredom when you are so actively involved. You may find your reaction to be just the opposite. Comprehension through listening naturally follows this kind of participation." *(Editorial, Ward E. Perrin, D.O., Illinois Med. J. 149:434, May, 1976)*

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager
London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS
Tel: 081 332 2422
Information was correct at t
to press 19th July 1994

Valium® (diazepam) has a range of clinical applications no other benzodiazepine can match

ROCHE

Indicated in anxiety, psychic tension and psychoneurotic anxiety with secondary depressive symptoms

A number of benzodiazepines can be used for treating anxiety. But Valium is the only one *specifically* indicated in such a wide range of situations where anxiety is clinically significant. For example, I.M. Valium is *specifically* indicated for anxiety prior to surgery. I.V. Valium is *specifically* indicated prior to elective cardioversion and as an adjunct prior to endoscopic procedures... and, it provides the added benefit of diminished patient-recall in these situations. When used orally as a psychotherapeutic agent, Valium is *specifically* beneficial for the muscular tension and other somatic and psychic symptoms of anxiety. And, it may also be used when psychoneurotic anxiety is accompanied by secondary depressive symptoms. It all comes down to this: *Valium–the benzodiazepine you know and trust–gives you a broader range of clinical utility than any other benzodiazepine.* And because adverse reactions more serious than drowsiness, fatigue and ataxia are rare, Valium is relatively safe. Do, however, caution patients against driving, operating dangerous machinery or the simultaneous drinking of alcohol. Also encourage patients to adhere to the prescribed dosage regimen or to discuss any needed adjustment with you.



Indicated adjunctively in skeletal muscle spasm and certain spastic disorders

Valium (diazepam) is the only benzodiazepine indicated in skeletal muscle spasm and spasticity. And here, too, its indications are extensive and quite specific: as an adjunct in skeletal muscle spasm due to reflex spasm to local pathology such as herniated disc or acute muscle strain; adjunctively in spasticity associated with paraplegia; adjunctively in spasticity due to cerebral palsy and athetosis; adjunctively in stiff-man syndrome and tetanus (the parenteral route only is used in tetanus).

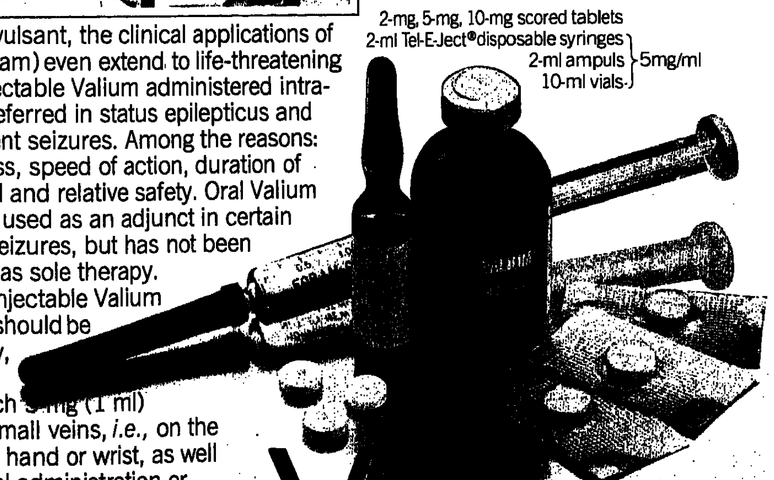
Valium can break the spasm/pain/spasm cycle, bringing more comfort and mobility to the patient with low-back syndrome. Valium can reduce involuntary movements, bringing more confidence and a boost in morale to patients with upper motor neuron disorders. It's *the one* benzodiazepine with clinically proven muscle-relaxant activity.

Indicated adjunctively in certain convulsive disorders



As an anticonvulsant, the clinical applications of Valium (diazepam) even extend to life-threatening situations. Injectable Valium administered intravenously is preferred in status epilepticus and severe recurrent seizures. Among the reasons: its effectiveness, speed of action, duration of seizure control and relative safety. Oral Valium has also been used as an adjunct in certain minor motor seizures, but has not been proved useful as sole therapy.

Whenever Injectable Valium is used I.V., it should be injected slowly, at least one minute for each 5 mg (1 ml) given. Avoid small veins, *i.e.*, on the dorsum of the hand or wrist, as well as intra-arterial administration or extravasation. Injectable Valium should not be mixed or diluted with other solutions or drugs and should not be added to I.V. fluids.



Valium® IV (diazepam) One of a kind.

Please turn page for a summary of product information.

Contacts:
Mark Rayner Managing Director
Julian Gorst Project Director
John McKee Project Manager
Vicki Morison Administration Manager
Isabel Hutchings Conference Manager
Charlotte Benton-Hughes Conference Assistant

London House
243-253 Lower Mortlake Road
Richmond
Surrey TW9 2LS

Tel: 081 332 2422

Information was correct at t
to press 19th July 1994

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets
2-ml Tel-E-Ject® disposable syringes
2-ml ampuls } 5mg/ml
10-ml vials }

- **the *one* benzodiazepine with *three* clinically useful pharmacologic properties**
- **a range of clinical applications unmatched by any other benzodiazepine**
- **dosage flexibility no other benzodiazepine can match**
- **a distinct pharmacokinetic profile that includes diazepam and three active metabolites**

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in: relief of skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome. *Oral form* may be used adjunctively in convulsive disorders, but not as sole therapy. *Injectable form* may also be used adjunctively in: status epilepticus; severe recurrent seizures; tetanus; anxiety, tension or acute stress reactions prior to endoscopic and surgical procedures; cardioversion.

Contraindications: Use of Injectable in infants and Tablets in children under 6 months of age; known hypersensitivity to drug; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: As with most CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Advise patients against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of their predisposition to habituation and dependence. Use of any drug in pregnancy, nursing women or in women of childbearing potential requires that expected benefit be weighed against possible hazard.

ORAL: Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral form adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may also be associated with temporary increase in frequency and/or severity of seizures.

INJECTABLE: *When used I.V., the following procedures should be undertaken to reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling, and, rarely, vascular impairment. Inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; extreme care should be taken to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs; do not add to I.V. fluids.*

Administer with extreme care to elderly or very ill and those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; resuscitative facilities should be available. When used with narcotic analgesic, eliminate or reduce narcotic dosage at least ⅓ and administer in small increments. Not recommended for OB use until additional information is available. Should not be administered to patients in shock, coma or in acute alcoholic intoxication with depression of vital signs.

Precautions: If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed or tolerated).

INJECTABLE: Laryngospasm and increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic and have necessary countermeasures available; hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly and debilitated; safety and efficacy in children under 12 not established.

Adverse Reactions: Side effects most commonly reported were drowsiness, fatigue and ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued.

Because of isolated reports of neutropenia and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy.

Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium (diazepam) therapy and are of no known significance.

INJECTABLE: Venous thrombosis and phlebitis at injection site, hypoactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia.

In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm and pain in throat or chest have been reported.

Dosage: Individualized for maximum beneficial effect.

ORAL—*Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg *b.i.d.* to *q.i.d.*; acute alcohol withdrawal, 10 mg *t.i.d.* or *q.i.d.* in first 24 hours, then 5 mg *t.i.d.* or *q.i.d.* as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg *t.i.d.* or *q.i.d.*; adjunctively in convulsive disorders, 2 to 10 mg *b.i.d.* to *q.i.d. Geriatric or debilitated patients:* 2 to 2½ mg 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg *t.i.d.* or *q.i.d.* initially, increasing as needed and tolerated (not for use under 6 months).

INJECTABLE: Usual initial adult dose is 2 to 20 mg I.M. or I.V., depending on indication and severity. Larger doses may be required in some conditions (tetanus). In acute conditions injection may be repeated within 1 hour, although interval of 3 to 4 hours is usually satisfactory. Lower doses (usually 2 to 5 mg) with slow dosage increase for elderly or debilitated patients and when sedative drugs are added. (See Warnings and Adverse Reactions.)

I.M. use: by deep injection into the muscle.

I.V. use: inject slowly, take at least one minute for each 5 mg (1 ml) given. Do not use small veins, i.e., dorsum of hand or wrist. Use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs; do not add to I.V. fluids.

Moderate psychoneurotic reactions, 2 to 5 mg I.M. or I.V. and severe psychoneurotic reactions, 5 to 10 mg I.M. or I.V., repeat in 3 to 4 hours if necessary; acute alcoholic withdrawal, 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary; muscle spasm, 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary

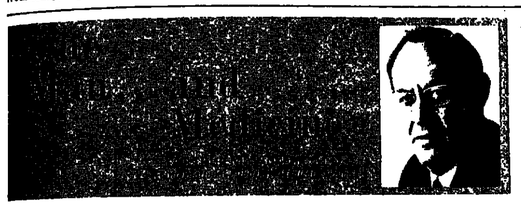
convulsive seizures, 5 to 10 mg I.M. or I.V. initially, repeat in 2 to 4 hours if necessary. In endoscopic procedures, titrate I.V. dosage to desired sedative response, generally 10 mg or less but up to 20 mg (if narcotics are omitted) immediately prior to procedure; if I.V. cannot be used, 5 to 10 mg I.M. approximately 30 minutes prior to procedure. As preoperative medication, 10 mg I.M.; in cardioversion, 5 to 15 mg I.V., within 5 to 10 minutes prior to procedure. Once acute symptomatology has been properly controlled with injectable form, patient may be placed on oral form if further treatment is required.

Management of Overdosage: Manifestations include somnolence, confusion, coma and diminished reflexes. Monitor respiration, pulse, blood pressure; employ general supportive measures, I.V. fluids, adequate airway. Immediate gastric lavage indicated for overdosage with tablets. Use levarterenol or metaraminol for hypotension, caffeine and sodium benzoate for CNS-depressive effects. Dialysis is of limited value.

Supplied: Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® (unit dose) packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Ampuls, 2 ml, boxes of 10; Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



Time To Listen

THIS IS the 150th anniversary year of the death of one of medicine's greats. In 1826 René Théophile Hyacinthe Laënnec died at age 45 of tuberculosis. His contribution to pathology is enshrined in the eponym, Laënnec's cirrhosis. His classic, Traité de l'auscultation médiate, *is a landmark in the physical diagnosis of mitral stenosis, pneumonia, pleurisy, emphysema and pneumothorax. It was in 1816 when Laënnec created the modern symbol of a physician, whose current version is now virtually a part of every doctor's "anatomy"—the stethoscope.*

It is fascinating to observe that Laënnec's great diagnostic breakthrough also marked the beginnings of the distancing of the physician. The stethoscope, in effect, was the first technologic interposition between patient and physician. This distancing grows with the explosive expansion of technology. As we seek more precise quantitation and greater objectivity, we lose what is probably one of the most important as well as the richest relationships that exist between the sick and those called to their care—human contact.

* * *

In commenting on a routine physical check-up, I observed the importance of understanding and tenderness, sensitivity and thoughtfulness of my doctor. I believe I am not alone in this respect. When patients unburden themselves, they indicate their need for a physician in whom they can find understanding as well as knowledge, tenderness as well as technology, insight as well as inspiration and, yes, importantly—the time to talk and the time to listen.

Distance/Closeness

The more I think about it, the more I appreciate the need to examine the problem, the paradox that even as the physician today can serve his patient better, the patient gets less of his physician than he has the right to expect.

Is it the physician's fault? In some part, yes. Is it the patient's fault? In some part, yes. Then what in heaven's name is the greatest part? The more I wrestle with this, the more I realize how we have contracted space and unhappily have contracted, not expanded time, and we have distanced the physician from the patient who so needs the feeling of "closeness" to his doctor.

* * *

For millennia the Hippocratic Oath, by and large, set the professional frame of reference for the physician-patient relationship. It remains a social verity today, but the rate of change which has so accelerated in the last hundred years, and more particularly in the last few decades, has created new situations that are disruptive to the historic physician-patient contact.

Medicine was originally available only to the few. Also, even as recently as a hundred years ago it was practiced in a social environment which changed little from that of the shaman and witch doctor, the rural physician or country doctor. The physician knew the patient and his family, he usually lived in the patient's village. There was a continuing and direct human contact. The doctor's senses monitored sight and sound.

Sight, Sound and Touch

Sight and sound and touch all played an important and historic part in the development of diagnosis, in an understanding of the clinical significance of fever and pulse in prognosis. The medical role of "touch" became enshrined in the miracles of the Gospel and later in the healing by "the king's touch." Closer to our day, we have the image of the country doctor seated gravely at the patient's bedside.

For thousands of years little really changed in man's mobility. Man first had to learn to domesticate animals and ride a horse. The horse, in turn, revolutionized warfare through the war chariot and cavalry, even as mobility has revolutionized medicine. In our rural society, the horse and buggy brought patient to doctor and doctor to patient. This form of out-reach extended medical care with relatively little disruption of physical contact or the environmental homogeneity of society. The automobile, the plane and the jet have changed all that. These, and the transistor, have altered both medicine, society and its environment for all time.

The Growing Separation

In medical technology, too, the first steps were small. The doctor placed his ear against the patient's back, chest or precordium. Then, after Laënnec, the physician was separated from his patient by the tube which was to become our "modern" stethoscope. Our eyes are also being replaced, first by fluoroscope and x-ray, and now by the incredible tri-dimensional body scanners. What a difference between the warm and reassuring touch of a considerate doctor about to percuss a chest and the cold, metalic contact with an x-ray cassette. This is a continuing escalation in the distancing of patient from physician by advancing technology and the demands implicit therein.

I am reminded of a story when I was interning in one of our city hospitals. A great English clinician had come to visit one of our important institutions, prestigious for its men of diagnostic acumen. A case was presented at bedside. The history was reviewed—in extenso; then the x-rays, blood counts, blood chemistries, SED rates, urines, ECGs and so on—test after test. The British visitor was most polite and heard it all out. When the presentation was finished, he had but one request.

"Could I, please, listen to the patient's heart?" he asked.

Oh! if we but had more time to listen.

Medicine on Stamps

Camillo Golgi



Camillo Golgi (1844-1926), for whom Golgi's cell was named, was born in Cortena, Italy. He received his M.D. from the University of Pavia in 1865, and after practicing medicine for 10 years returned to the university where he spent the rest of his life doing research in neuroanatomy. He developed the silver chromate stain for nerve tissue, and made other contributions to the fundamental knowledge of nerve tissue. He was a co-winner, with Ramon y Cajal, of the Nobel Prize in Medicine and Physiology in 1906.

Text: Dr. Joseph Klar
Stamp: Minkus Publications, Inc., New York

Testosterone and Estrogen Both Linked to Cardiovascular Disease

Continued from page 3

study were less than 44 years of age," the investigator added, "the reported increase in plasma-estrogen concentration with aging in men suggests that hyperestrogenemia might persist or even develop as risk factor in older men."

In the first of Dr. Ramwell's studies, arterial occlusive thrombosis was induced by inserting loop-shaped cannulas into the abdominal aortas of 229 Wistar male and female rats aged one-and-a-half, three, four, six and 12 months. Reporting in *Nature* (June 24, 1976), Dr. Ramwell found that the mortality rate of animals three, four or six months of age was approximately twice as high in male rats as in females, the rate increasing with the age of the animal. In addition, statistically significant differences were found in the size of the thrombi between male and female rats at the age of three, four and six months. Finally, obstruction time differed between the sexes at the ages of three, four and six months.

To determine whether species differences were significant in the incidence of thrombus formation, a second study was conducted on 27 six-month-old male and female New Zealand rabbits. Thrombi were found in 90.9% of the male and 56.2% of the female rabbits.

Mortality Increased

In a third study, the effects of testosterone and estradiol were observed in 194 three-month-old Wistar male and female rats with induced occlusive arterial thrombosis. Mortality rate, dry thrombus weight and obstruction time were determined. "Testosterone treatment increased the mortality rate more than fourfold in male as well as female rats," Dr. Ramwell stated. Estradiol treatment showed a tendency toward a decrease in mortality, he added, but "this effect was not statistically significant."

In a final experiment in the series, a non-steroidal anti-androgen was given in combination with testosterone to male and female rats with induced thrombosis. "The anti-androgen significantly decreased the mortality rate of both male and female rats when treated with testosterone," Dr. Ramwell reported.

'No Conflict'

In an interview, Dr. Ramwell emphasized that there is "no conflict at all" between his findings and those of Dr. Phillips, adding, however, that "another five years of work is before us. It is difficult to correlate these things."

Dr. Harriet P. Dustan, president-elect of the American Heart Association, said she would prefer to take a "wait and see attitude" on the role of testosterone.

There have been so many conflicting studies concerning sex hormones that "It is difficult to know what effect any of them may have," she commented.

Dr. Sanford Wessler, Professor of Medicine and Associate Dean at the New York University Postgraduate School of Medicine and author of a paper on estrogen and clot formations said, "I think there is increasing evidence that the administration of exogenous estrogen may have a temporal correlation with the development of thrombosis."

Neurotoxin In Cheese

Medical Tribune World Service

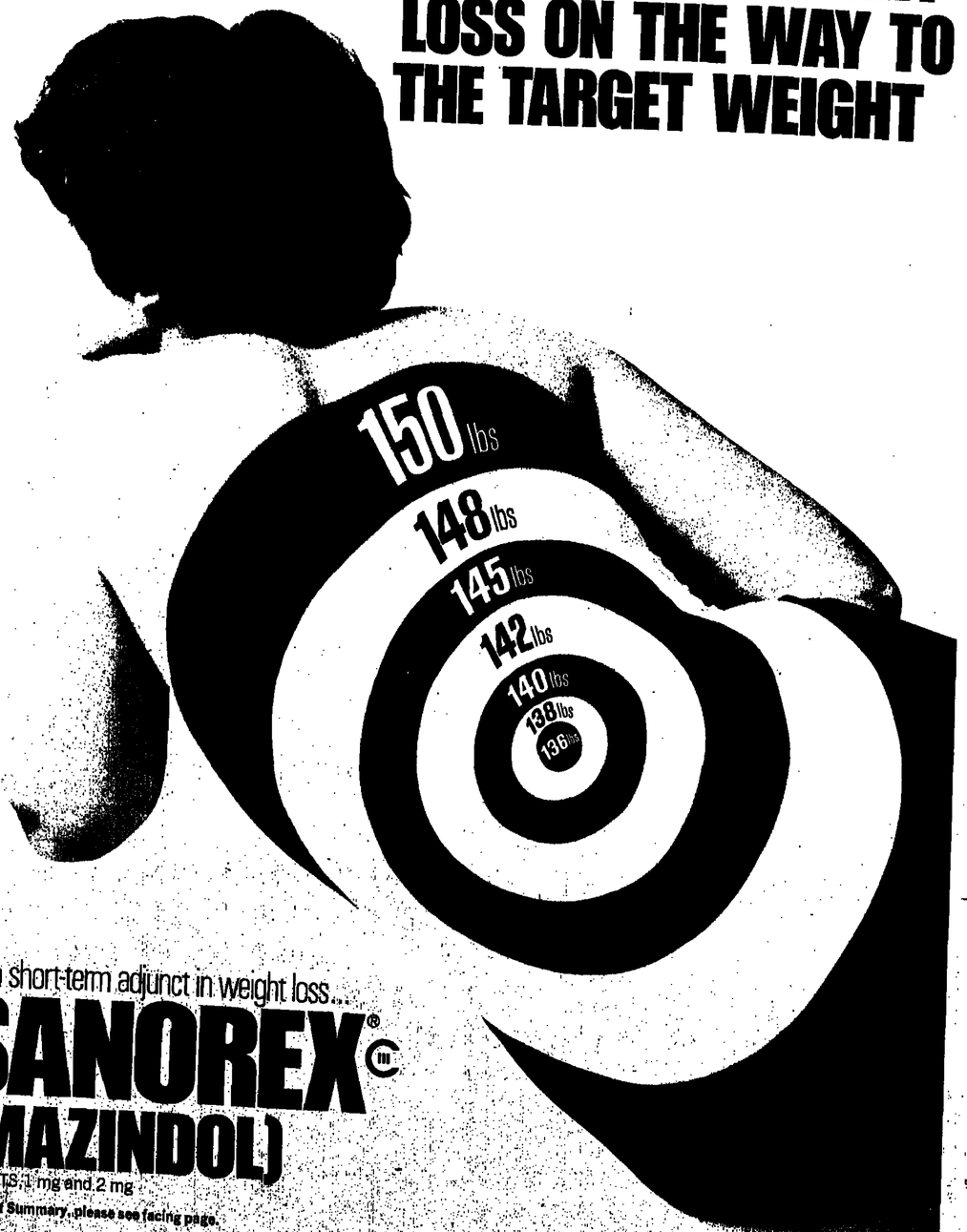
OTTAWA, CANADA—Government researchers here have identified a neurotoxin in blue cheese, roquefortine, which causes convulsive seizures in mice. Dr. Peter M. Scott and Dr. Barry P. C. Kennedy, of the Bureau of Chemical Safety Food Directorate said that the alkaloid substance is a natural product of the mold that gives roquefort, stilton, and gorgonzola cheeses their characteristic color and flavor.

EPIGRAMS—Clinical and Otherwise

The great tragedy of Science—the slaying of a beautiful hypothesis by an ugly fact.

Thomas Henry Huxley (1825-95)
Collected Essays, "Biogenesis and Abiogenesis"

CONSISTENT WEIGHT LOSS ON THE WAY TO THE TARGET WEIGHT



As a short-term adjunct in weight loss...

SANOREX®C III

(MAZINDOL)

TABLETS, 1 mg and 2 mg

For Brief Summary, please see facing page.

SANOREX®C III

(MAZINDOL)

TABLETS, 1 mg and 2 mg

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given a pressor amine agent (e.g., levarterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: An increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses.

Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. *Cardiovascular:* Palpitation, tachycardia. *Central Nervous System:* Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. *Gastrointestinal:* Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. *Skin:* Rash, excessive sweating, clamminess. *Endocrine:* Impotence, changes in libido have rarely been observed. *Eye:* Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg. three times daily, one hour before meals, or 2 mg. once daily, one hour before lunch. The lowest effective dose should be used. Should GI discomfort occur, mazindol may be taken with meals.

Overdosage: There are no data as yet on acute overdosage with mazindol in humans. Manifestations of acute overdosage with amphetamines and related substances include restlessness, tremor, rapid respiration, dizziness. Fatigue and depression may follow the stimulatory phase of overdosage. Cardiovascular effects include tachycardia, hypertension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting and abdominal cramps. While similar manifestations of overdosage may be seen with mazindol, their exact nature have yet to be determined. The management of acute intoxication is largely symptomatic. Data are not available on the treatment of acute intoxication with mazindol by hemodialysis or peritoneal dialysis, but the substance is poorly soluble except at very acid pH.

How Supplied: Tablets, 1 mg. and 2 mg., in packages of 100.

Before prescribing or administering, see package circular for Prescribing Information.

BAN 6-874

SANDOZ PHARMACEUTICALS, EAST HANOVER, N.J. 07936

Second Countersuit by MD Challenges Wilful 'Shotgun' Malpractice Claims

Continued from page 1

cutdown in order that blood could be administered.

Both physicians were dismissed as defendants by Circuit Court Judge David A. Canel but they have insisted on taking action against Mr. Demos for "wilfully and wantonly" naming them.

Eugene L. Shepp, attorney for the two physicians, said the suit was filed "for the obvious reasons that neither of my clients had anything to do with the treatment of the patient's medical condition which ultimately may have caused her death.

"This is a classic example of the shotgun approach where many defendants are indiscriminately named in the hope that someone may be found liable. Such a practice of naming multiple defendants without reasonable cause is not in the best interest of the legal profession, the medical profession or the general public and must be stopped."

Each physician is asking $65,000 in damages, charging that their reputations were injured and their licenses to practice medicine placed in jeopardy by the suit.

In addition to the 20 doctors and nurses, Mr. Demos named the Skokie Valley Community Hospital as defendant in the malpractice suit filed on behalf of Noel Murtagh, husband of the deceased woman. Mr. Murtagh also is named as a defendant in the Skokie physicians' counter-suit.

Interest Continues

Meanwhile, interest in the victorious countersuit brought by Dr. Berlin has abated but little. The letters and calls continue to arrive, not only from the medical profession but also the general public.

"I believe the reasons are varied," he said. "There are over 300,000 physicians in the nation and they all have friends, relatives and patients. So there are a lot of people who are concerned with malpractice and with the frustration on the part of these doctors in not having been able to strike back.

"A more important reason, perhaps, is that I represented the 'underdog,' a man fighting against a bad system. I fought for what I thought was a just cause, and I did what many others have wanted to do but couldn't. And I won. And I think the American public simply likes that."

Dr. Berlin had been sued for $250,000 by a 40-year-old woman, a neighbor and casual acquaintance, who had charged him with negligence in the reading of an x-ray of her little finger injured in playing tennis.

She dropped the suit on her attorneys' advice but Dr. Berlin refused to drop his countersuit asking a "symbolic" $3,000. The jury awarded him $8,000 after deliberating only 15 minutes.

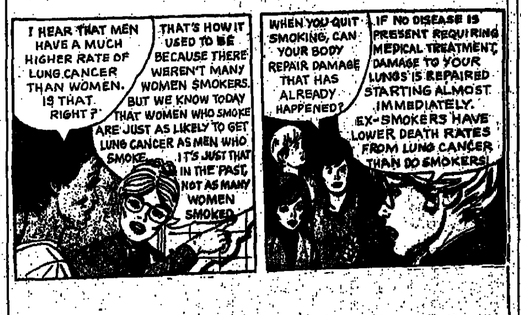
His total costs were $5,000, which the Hartford Insurance Company paid. The two legal expert witnesses, Charles O'Laughlin and Bruce Hoff, and the Hartford attorney, Fred Grossman, who spent three full days on his own time at Dr. Berlin's side during the trial, all refused to bill him because of their interest in the case "on principle."

In addition to charging the woman's husband, an attorney, with involving him in litigation without reasonable cause, Dr. Berlin accused the husband of violating the barratry statute in Illinois. This was dismissed by the court on the grounds that barratry was a criminal offense and as such would have to be brought by the States Attorney's office and not by an ordinary citizen in civil court.

Would Dr. Berlin go through it again? During the episode, there were times when the long hours in the law library and the interruptions in his professional and family life made him feel he wanted to give up the whole thing.

"But now that it is over, and seeing the response that has been generated, I most certainly would do it again," he said. "And I would encourage anyone else to do the same, provided he had a good case, a good lawyer, perseverance and a high tolerance for frustration."

Anti-Smoking Comic Book



"Cigarettes are okay—for losers!" conclude teen characters in a new anti-smoking comic book being distributed by the American Cancer Society. A major aim is to reduce the number of girl smokers, which, ACS says is on the rise.

Pediatric Progress

. . . presenting excerpts from current journal articles and commentaries of interest to physicians who treat children.

Boys and Burns

"The number of boys who climb power poles and escape injury is unknown, as is the number of these boys who are electrocuted annually. However, in the broader context, a National Safety Council, five-year, nationwide 'Survey of Non-Employee Overhead Electrical Contacts,' reported 865 deaths and 3,652 nonfatal injuries from overhead power lines among people not employed by a utility company.[7] Ninety-three per cent of these victims were male. Approximately 40% of 981 non-work-connected incidents involved children between 9 and 18 years of age.

"The prevention of high-tension accidents might follow the example of preventive strategies directed at fabric ignition burns. Groups interested in preventing such burns have sought to legislate product changes (flame-retardant mattresses and children's sleepwear) and to educate the public in avoiding burn hazards and in making appropriate emergency responses (rolling on the ground to smother burning clothing). With respect to electrical burns, communities can legislate that all new power lines be buried, and that open wires, "live" rails, and transformer substations might be made less accessible." (*Elizabeth McLoughlin, M.A., Michael P. Joseph, A.B., and John D. Crawford, M.D., J. Pediat. 89:63, July, 1976*)

Children and Funerals

"Although no specific post-funeral syndrome seems to exist, many, if not most, children under the age of six or seven seem not benefited psychologically by attending a funeral. Although some young children can tolerate funerals well if sensitively supported by their parents, the fact is that such support is more often absent than present. One useful indicator of the parents' ability to make the funeral experience a positive one is whether or not the child wishes to attend. A child, no matter how young, who feels secure in attending should usually do so. Conversely, a child who refuses or is steadfastly reluctant to attend a funeral is usually perceiving accurately his parents' inability in their own mourning to provide him with adequate support for this emotionally charged endeavor." (*John E. Schowalter, M.D., J. Pediat. 89:139, July, 1976*)

Steroid Action In RA

Medical Tribune World Service

LONDON—Research by G. P. Lewis, Ph.D., and Priscilla J. Piper, Ph.D., of the Royal College of Surgeons, suggests that the effectiveness of steroids in combatting inflammatory diseases may be due to inhibition of prostaglandin production, thought to be involved in the development of rheumatoid arthritis, osteoarthritis, bursitis, gout, asthma and severe psoriasis.

Field Trials of Swine Flu Vaccine Used Texas State Inmates Despite Federal Ban

Continued from page 1

cine may be as much as 90% effective in adults. Efficacy rates for children have not been established as of yet, he noted.

According to top HEW physicians, the swine-type virus, which caused the death earlier this year of an 18-year-old Fort Dix Army recruit, had not been since in the general population since 1930.

"The entire population is immunologically vulnerable," Dr. Cooper stressed.

Asked by Dr. Sackler about the morality of a nationwide vaccination program, Dr. Cooper replied: "An epidemic would threaten all age groups . . . The actual number of complicated cases would be sufficiently high in an epidemic situation to warrant immunization of all persons who are medically able to take the vaccine."

Dr. Cooper rejected the suggestion that the administration of the vaccine to the general population could be considered an experiment, and predicted that the vaccination program would be "immensely valuable in developing effective disease prevention and control programs in other areas."

Finally, Dr. Cooper emphasized that the decision to launch the nationwide program was not made solely on the basis of opinions from federal officials.

"From the beginning, we consulted with dozens of experts on influenza and vaccines about the significance of the findings at Fort Dix and the course of action which those findings suggested," he said. He added, "Even the President did not announce his decision to accept our recommendation for a national program without first personally asking 30 experts for their consensus at a meeting held at the White House."

Medical Meeting Schedule

Sept. 3 American Chemical Society, *San Francisco, Calif.*
Sept. 3-4 American Medical Association, *Jackson Hole, Wyo.*
Sept. 5-11 Interamerican Congress of Cardiology, *Caracas, Venezuela*
Sept. 9-11 American Association for the Surgery of Trauma, *Colorado Springs, Colo.*
Sept. 10-12 ...AMA Regional Meeting, *Portsmouth, N.H.*
Sept. 11-16 ...World Federation on Neurology, *Hague, Netherlands*
Sept. 13-16 ...American Academy for Cerebral Palsy, *Los Angeles, Calif.*
Sept. 13-14 ...3rd Mid-Western Regional Congress, *Detroit, Mich.*

Diuretics Cited as Risky in Normal Pregnant Women

Continued from page 3

- Incidence of induction of labor, need for stimulation of labor after spontaneous onset of labor, uterine inertia and meconium staining were all significantly higher among mothers taking diuretics.
- Incidence of stimulation of labor and uterine inertia were even higher when the mother received a diuretic prescription within six weeks of delivery.
- Length of labor was significantly longer for women in the diuretic group.

Data for the study were based on an ethnically divergent obstetrical population compiled during 1959-1967 at the Child Health and Development Studies section of Berkeley's School of Public Health, said Ms. Christianson. Diuretics, primarily thiazide derivatives, had been prescribed for edema, excess weight gain or other symptomatic complaints.

Higher incidences of induction and stimulation of labor, uterine inertia and meconium staining were "unexpected findings," the investigators said.

Although edema, heavier birth weights, and obesity in the diuretic group might account for some of the findings, "The fact that a chemically related drug, diazoxide, which is not a diuretic, will cause a cessation of labor, presumably by a direct action on smooth muscle, suggests that thiazide diuretics may possess some of this activity," the team said.

Ms. Christianson noted that "The need to control for gestational age in examining such events as edema or the use of diuretic drugs, both of which are linked to gestational age itself, is of paramount importance." When data are so controlled, "There is no increased perinatal mortality associated with untreated maternal edema. This finding makes the diuretic drugs suspect.

"The findings support the contention that higher risks are associated with one or more factors differentiating the two groups, namely, edema, undefined factors associated with edema, or the consumption of a diuretic drug," the team concluded.

While they may all need multivitamins—

CAN YOU MATCH THE SPECIAL VITAMIN NEEDS

SPECIAL VITAMIN NEEDS	PATIENT
1. B-complex, C	
2. B_1, B_6, folic acid	
3. A, B-complex, C	
4. B_6, folic acid	
5. A, C	
6. C, D	

Matching the special vitamin needs to the patient. Like most physicians, it's something you probably do every day. Because for certain patients, vitamins often provide valuable nutritional support during therapy. Single or multivitamin supplements, carefully calibrated to ensure that the patient is receiving *balanced* amounts of vitamins, and the recommendation of adequate minerals as well, may be needed to prevent or correct nutritional inadequacies—to facilitate wound healing—to forestall potential nutritional problems.

Unfortunately, a number of patients who need vitamin supplements may never receive them. These are the patients who appear to be adequately nourished and who honestly believe that they're eating sensibly. But their knowledge of what constitutes good nutrition may well be on the sketchy side. And they may have been eating poorly balanced meals for most of their adult lives...

Which explains why more and more physicians are now beginning to probe into their patients' eating habits whenever they take medical histories. And why they're providing much more guidance and counsel than ever before in nutritional areas.

Because when you think about it—it clearly makes good sense to correct vitamin inadequacies. And even better sense to correct them *before* they become clinically apparent.

ROCHE

Roche Chemical Division, Hoffmann-La Roche Inc., Nutley, N.J. 07110

GOOD NUTRITION OFTEN STARTS RIGHT IN YOUR OFFICE.

ANSWERS: ٢ ٤ ١٠ ٦ ١١ ٥ ٣ ٩ ٨ ٧

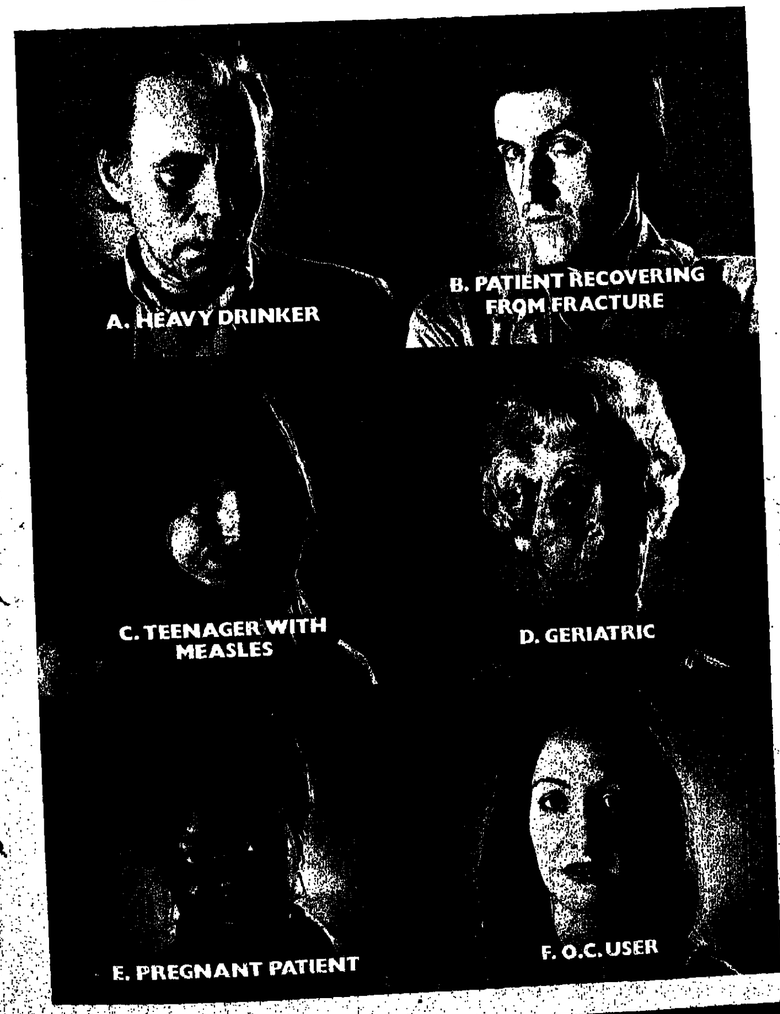
RCD 1559

Clinical Trials

By Oldden



WITH THESE PATIENTS?



IMMATERIA MEDICA

Nanny Advert

Dear Sir,

I am a doctor's daughter seeking employment as a qualified Nanny in the United States, preferable on the West Coast.

I understand that it may be possible for you to insert an advert stating the above. If this is possible, could you write to the above address stating the charges for such an advert?

Yours faithfully,
HELEN SMITH
6, Queens Road
Datchet, Slough
Berkshire, SL3 9BN

No charge! We trust the line will form to the right, all the way from California.

Hearings Heard

When Secretary of the Treasury Simon was testifying on revision of estate taxes, he referred to a proposed marital deduction as "a free interspousal transfer." And this prompted Kansas Senator Dole's question: "You mean wife-swapping?"

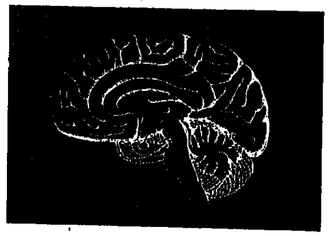
We'll get on with the chaos by reporting that one of the witnesses testifying in favor of comprehensive national health insurance, asked: "Who is Aristotle? And what does he have to do with national health insurance?"

We never did hear the answer from the witness, but Cary J. Kuhlmann, of the Orleans Parish Medical Society in New Orleans, where a subcommittee held hearings, sent us the response of Dr. Donald J. Palmisano. He spoke for the Society, citing something written in 335 B.C. by a physician's son:

"We observe that persons of experience are actually more successful than those who possess theory without experience. The reason of this is that experience is acquaintance with individual facts but art with general rules, and all action and production is concerned with the individual. Hence, if one possesses theory without experience, and is acquainted with the universal concept, but not with the individual facts contained under it, he will often go wrong in his treatment; for what has to be treated is the individual."

And guess who was the physician's son, asks Dr. Palmisano. "Aristotle."

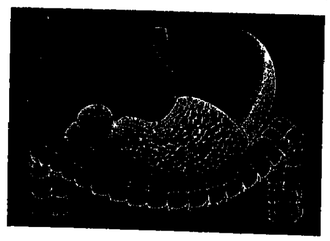
Are all antianxiety-anticholinergic therapies the same?
Not if you know Librax®.



Only Librax provides

■ **the well-known antianxiety action of Librium®** (chlordiazepoxide HCl)

plus



■ **the prompt antisecretory-antispasmodic action of Quarzan®** (clidinium Br)

with the convenience and economy of a single medication... all advantages in sustaining patient compliance

adjunctive dual-action

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

For relief of psychovisceral symptoms in irritable bowel syndrome* and duodenal ulcer*

A distinctive antianxiety-anticholinergic agent

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium® (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacologic effects of agents, particularly potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are avoidable in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis); jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of the mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Tribune Economic Analysis



Economy Slowed By High Costs in Building Industry

BY ELIOT JANEWAY
Canadian Economist

One good reason for the stepped-up flow of money into New York in the face of the drop-off in interest rates is the revitalization of the stock market. New York stock prices are going up much faster than interest rates are coming down.

But despite the welcome relief from high costs and low confidence signaled by the drop in interest rates, the American economy is still being held back by the persistent depression in its biggest single business: home building and buying. The cost of shelter is far and away the largest single item in representative family budgets. The failure of the building business to participate in the recovery is the direct cause of a pernicious backlash from inflation. The prices of existing homes, as well as rents, are in for a steep rise, which has already begun.

Several obstacles still stand in the way of the full-fledged recovery in home building. Fuel costs have stopped rising, but they are still too high for builders to take with comfort. Utility rates are headed painfully higher. Property taxes are now jumping faster than a hyped-up kangaroo; tenants suffer living-cost hikes, too, when their landlords are hit with tax increases.

But the most troublesome obstacle in the way of a home-building revival is the high cost of mortgage money. Mortgage rates running up to 15% are not the only factor; the rigidity of mortgage money costs is inflicting an even greater hardship on borrowers and lenders alike.

Money market forces are not the only pressures responsible for mortgage rates; the formidable body of statutory and regulatory restrictions is just as influential. If only money market forces were at work in the Main Street mortgage market, millions of families now locked into home-financing costs they cannot afford would be enjoying substantial relief.

At the worst of the spring credit crunch scare, long-term bond yields did not rise. Now short-term rates are making money a giveaway for big government and business borrowers. The suspicion is unavoidable that our way of handling the business most costly to every household in the country is the wrong way.

Ask Janeway

In trying to follow your recommendation for accumulating utility preferreds yielding over 11%, I could get only a very limited list from my broker. Can you suggest somewhere else I might go for this information and comment on my broker's question: "Why not a little less yield and more capital gains?"
VA Doctor

Ask your broker to refer your question to one of the Wall Street firms making markets in utility preferreds. The risk-reward ratio is never favorable to gains players when yields rise on fixed-income securities. But when these yields fall, the investor in income is "stuck," as they say on Wall Street, with a quick profit as well as a high yield. Only brokers who follow the pack believe in the conflict between high yield and big gain implicit in your question.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, *880 Third Avenue, New York, N.Y. 10022.*

In cerebral and peripheral ischemia associated with arterial spasm

Cebral® 100 mg capsules
ethaverine HCl

In cerebral ischemia:
direct vasodilation of cerebral vessels; virtually no CNS effect; rare incidence of side effects permits long-term use

In peripheral vascular disorders:
relaxes smooth muscles of larger blood vessels by direct effect unrelated to muscle innervation

For additional product information and professional samples, write on your letterhead to
Professional Service Department
KENWOOD LABORATORIES, INC.
New Rochelle, New York 10801

Indications: For the relief of cerebral and peripheral ischemia associated with arterial spasm.

Contraindications: The use of ethaverine hydrochloride is contraindicated in the presence of complete atrioventricular dissociation.

Precautions: Use with caution in patients with glaucoma. Hepatic hypersensitivity has been reported with gastrointestinal symptoms, jaundice, eosinophilia and altered liver function tests. Discontinue drug if these occur.

The safety of ethaverine hydrochloride during pregnancy or lactation has not been established; therefore it should not be used in pregnant woman or in women of childbearing age unless, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Adverse Reactions: Although occurring rarely, the reported side effects of ethaverine include nausea, abdominal distress, hypotension, anorexia, constipation or diarrhea, skin rash, malaise, drowsiness, vertigo, sweating, and headache.

Dosage and Administration: One capsule three times a day.

How Supplied: 100 mg capsules in bottles of 50 and 500.

I·L·X B12™

hematinics of choice

for nutritional and iron deficiency anemias

By teaspoon or tablet
- Readily assimilated
- Well tolerated
- Economical

Usual Dosage: ELIXIR—1 to 3 teaspoonful daily or as directed by physician.
TABLETS—1 tablet 3 times a day or as directed by physician.
Supplied: 12 ounce bottles of Elixir. Bottles of 100 tablets.

I·L·X B12™
Elixir—each ounce represents: Iron and Ammonium Citrate 18 gr. • Liver Fraction 1 4 gr. • Thiamine Hydrochloride 10 mg. • Riboflavin 4 mg. • Niacinamide 20 mg. • Cyanocobalamin (Vit. B12) 20 mcg. • Alcohol 8% by volume.
Tablets—each tablet contains: Vitamin C 60 mg. • Cyanocobalamin (Vit. B12) 10 mcg. • Folic Acid 1 mg. • Ferrous Fumarate 200 mg. (Iron 66 mg.) • Thiamine Hydrochloride 10 mg. • Riboflavin 10 mg. • Niacinamide 100 mg.

Kenwood Laboratories, Inc., New Rochelle, New York 10801
developers and suppliers of Cebral® and Kengesin®

MDs Programmed for Self-Destruction?

Medical Tribune World Service

DUBLIN—Are physicians genetically programmed for self-destruction?

Dr. Norman Moore, a psychiatrist from Trinity College, Dublin, thinks so. He told a joint meeting of the British, Irish and Canadian Medical Associations here that the extremely high suicide rate in the medical profession throughout the world suggests that physicians are genetically pre-ordained to "melancholia or involutional depression." He added that the fact that medical students also have a higher suicide rate than other students do supports the notion that there must be a common personality flaw behind the self destruction syndrome, rather than the rigors of the profession itself.

"Paradoxically, the people most prone to this form of depression were often those with warm, outgoing personalities, the doers, rather than the thinkers, apparently stable, mature, well integrated, dynamic and ambitious people. These are the very sort that are attracted to medicine and most valuable in the medical and other service professions," he said.

Bactrim™ DS

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

double strength tablets

Just 1 tablet b.i.d. for better patient compliance

For chronic or frequently recurrent urinary tract infection.



Just 1 tablet b.i.d.

When the patient with chronic or frequently recurrent urinary tract infection fails to comply with therapy, persistent bacteriuria or relapse may occur. Single tablet b.i.d. dosage makes compliance easier.

Same efficacy with half the number of tablets

Studies have established bioequivalency of Bactrim DS double strength tablets with the Bactrim single strength tablets.

Greater economy for patients

Fewer tablets per day offer sufficient medication for the full course of therapy at a lower cost to the patient.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli, Klebsiella-Enterobacter, Proteus mirabilis; Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register*, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole —bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored—bottles of 16 oz (1 pint).

Bactrim™ DS

double strength tablets

(160 mg trimethoprim and 800 mg sulfamethoxazole)

For chronic cystitis and pyelonephritis evidenced by persistent bacteriuria and due to susceptible organisms

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110